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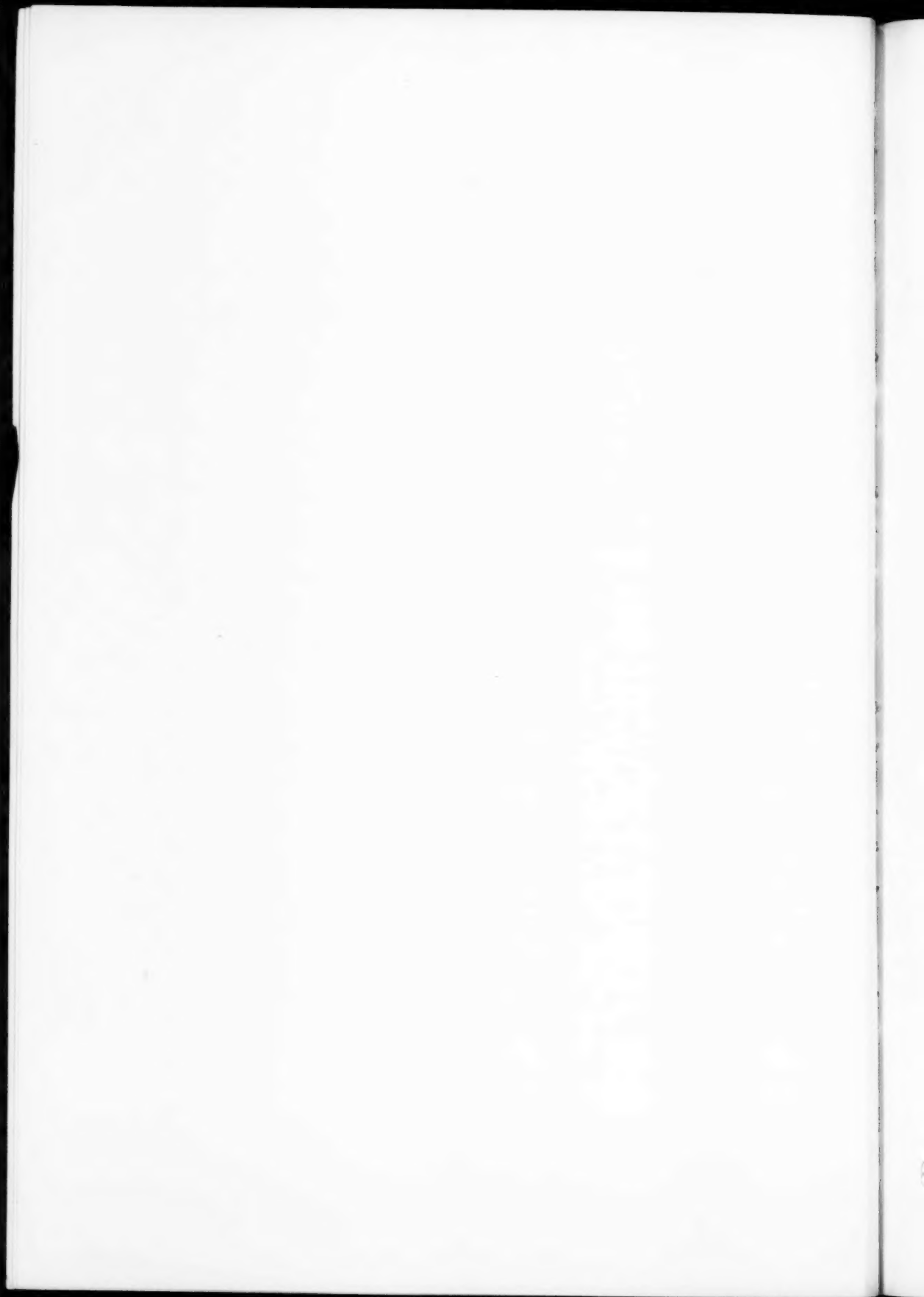
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THE PILGRIM STATE HOSPITAL*

BY FREDERICK W. PARSONS, M. D.

COMMISSIONER, NEW YORK STATE DEPARTMENT OF MENTAL HYGIENE, ALBANY, N. Y.

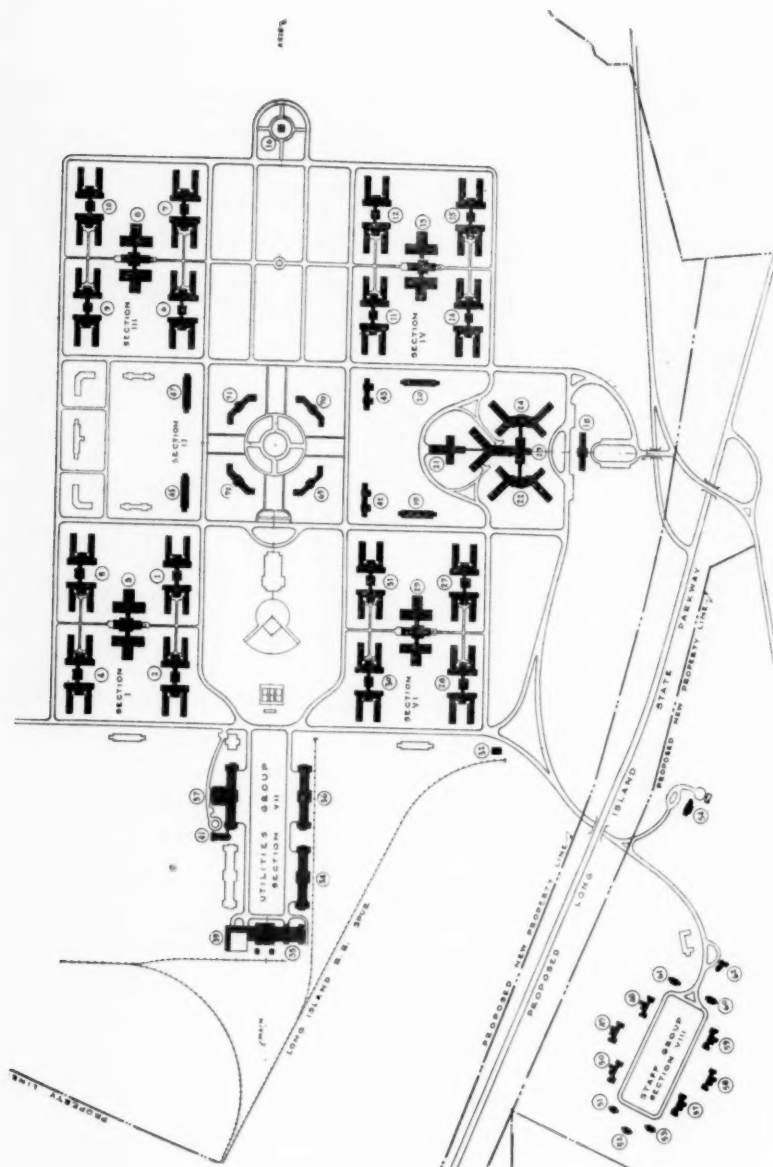
New York State needed a new institution to accommodate mental patients in the rapidly growing district about New York City. Existing demands were with difficulty being met by four hospitals, a fifth of moderate size (3,500) was in the course of construction, and there were good reasons to believe that one out-moded hospital on land owned by New York City might have to be abandoned within a few years. That was the situation in 1927 when a new mental hospital was being considered.

The size of the institution was a matter of grave concern. Should several small hospitals be built or one sufficiently large to meet the need as then visualized. A demand for ten thousand beds could be foreseen but that number was not required when these decisions were being made so it was determined to build an institution to comprise an intensive treatment group which would include a reception building, a diagnostic center and a general hospital for the acutely sick and four continued treatment groups, each accommodating 1,500 patients.

How large a mental hospital should be, for many years, has been a topic of contention and old copies of the *American Journal of Insanity* contain interesting points of view, modified as time went on, and fairly complete accounts of the discussion provoked. In 1850 it was thought that "the highest number that can be with propriety treated in one institution is 250, while 200 is the preferable maximum," and in 1866, it was said that "the enlargement * * * * may properly be carried to the extent of accommodating 600." By 1908, 1,200 to 1,500 was thought possible, but 1,000 was preferable, yet there were those who advocated larger institutions. The proponents of the large and of the small hospital had arguments which merit consideration but in the main those who proposed the smaller units seem to have given little consideration to the necessity of accommodating large numbers. A hospital should be sufficient for the present demands and those foreseen for the immediate future and no larger. Con-

* Published also in the *American Journal of Psychiatry*.

THE PILGRIM STATE HOSPITAL



PLOT PLAN OF PILGRIM STATE HOSPITAL

struction in excess of requirements is wasted space and a hospital smaller than conditions require leads to subsequent enlargement, likely to be disorderly, overcrowding or duplication. Fortunately the New York State Department of Mental Hygiene had considerable information at its disposal and it was possible to arrive at an understanding of the present needs, and there was experience on which to predict, with reasonable certainty, the demands to be made upon a projected hospital in the near future.

While the first year admissions to a new hospital were not likely to number 2,000 patients, experience had shown a gradually increasing admission rate which would soon reach that figure. As the average hospital residence is about five years it was apparent that the institution should be five times the admission rate. Deaths and discharges would then provide room for the admissions.

Where should the new institution be located? Westchester County is that portion of New York State, east of the Hudson River, immediately north of New York City. It contains large estates, thriving towns, and a considerable portion of the county is a watershed for New York City. To all but sanitary engineers there are esthetic objections to locating large institutions on a watershed. Rockland County, on the opposite side of the Hudson River, is also north of New York City, but it presents water supply and sewage disposal difficulties not easily overcome. The logical location seemed to be Long Island and an 1100-acre site was secured in Suffolk County approximately 35 miles from New York City. Long Island winters are relatively mild, the soil is sandy, excellent water from wells is available in unlimited quantities and sewage is disposed of easily. The railroad transportation facilities are good and there are large tracts of level land, presenting no foundation difficulties, upon which an orderly arrangement of large groups of buildings is possible. The new institution was therefore located on Long Island, and in honor of Dr. Charles W. Pilgrim, who for many years had served the State of New York and prior to retirement had been a State Hospital Commissioner, the institution was named the Pilgrim State Hospital.

For several years a committee of New York State institutional superintendents had considered types of structures suitable for

patients, employees and officers and had adopted standard buildings. In planning the Pilgrim State Hospital this Department therefore had the benefit of their deliberations. A bureau of research, established by the Division of Architecture, had excellent data and Mr. William E. Haugaard, the State Architect, with his co-workers, was most helpful. All shared with the Department of Mental Hygiene a desire to make the new institution a useful, workable, economic unit.

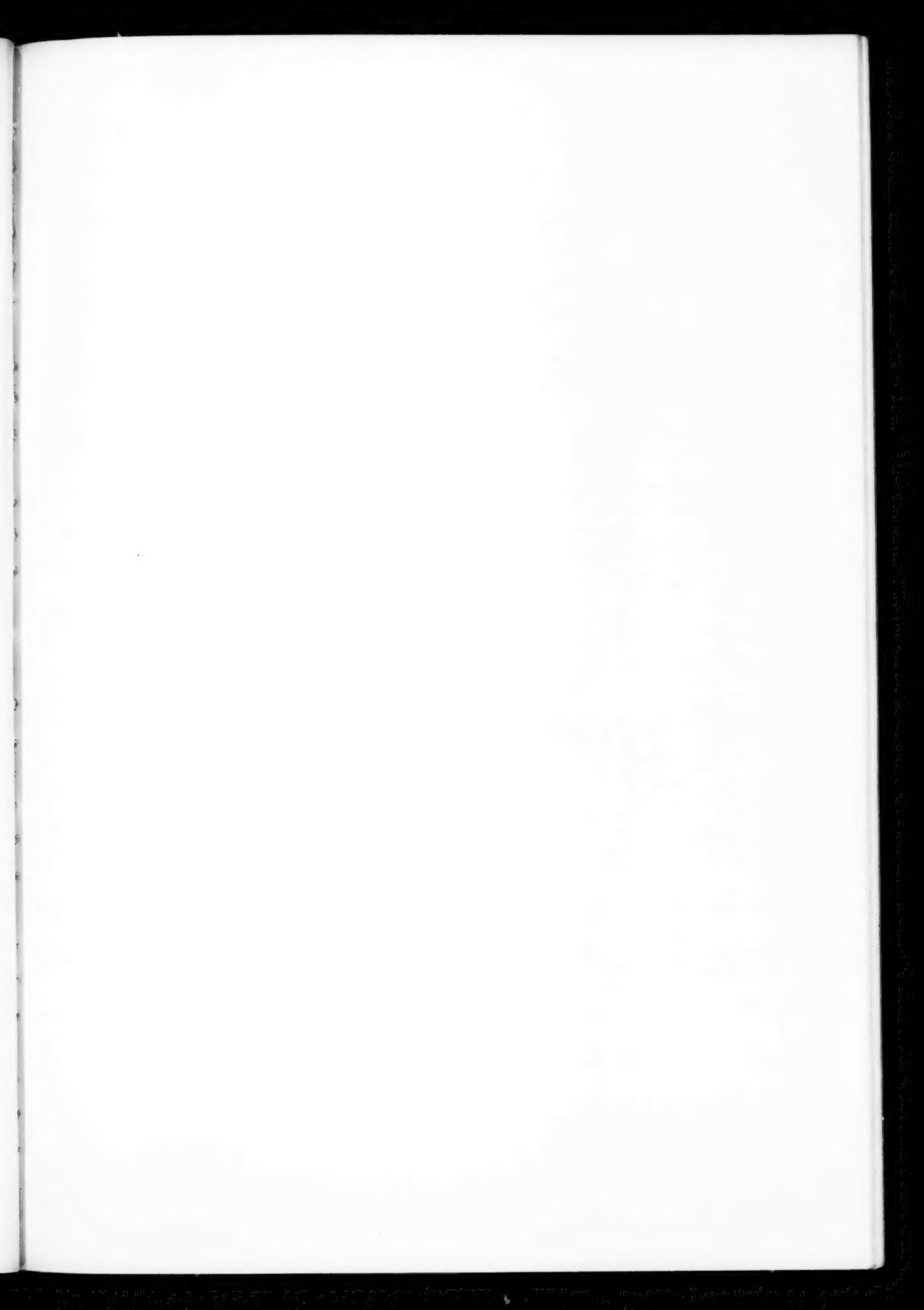
Admissions from metropolitan areas with large foreign groups differ from those originating in smaller centers of population of racial homogeneity and a survey indicated the classification shown below to be desirable.

	Per cent
Reception group	10.0
Depressed and disturbed	22.5
Quiet and moderately disturbed	50.0
Feeble	12.5
Tuberculous	3.5
Acute medical and surgical	1.5
	<hr/>
	100.0

As the other institutions serving New York City were overcrowded with residual continued treatment cases, and greatly needing relief, the first contracts were for buildings to care for the continued treatment cases.

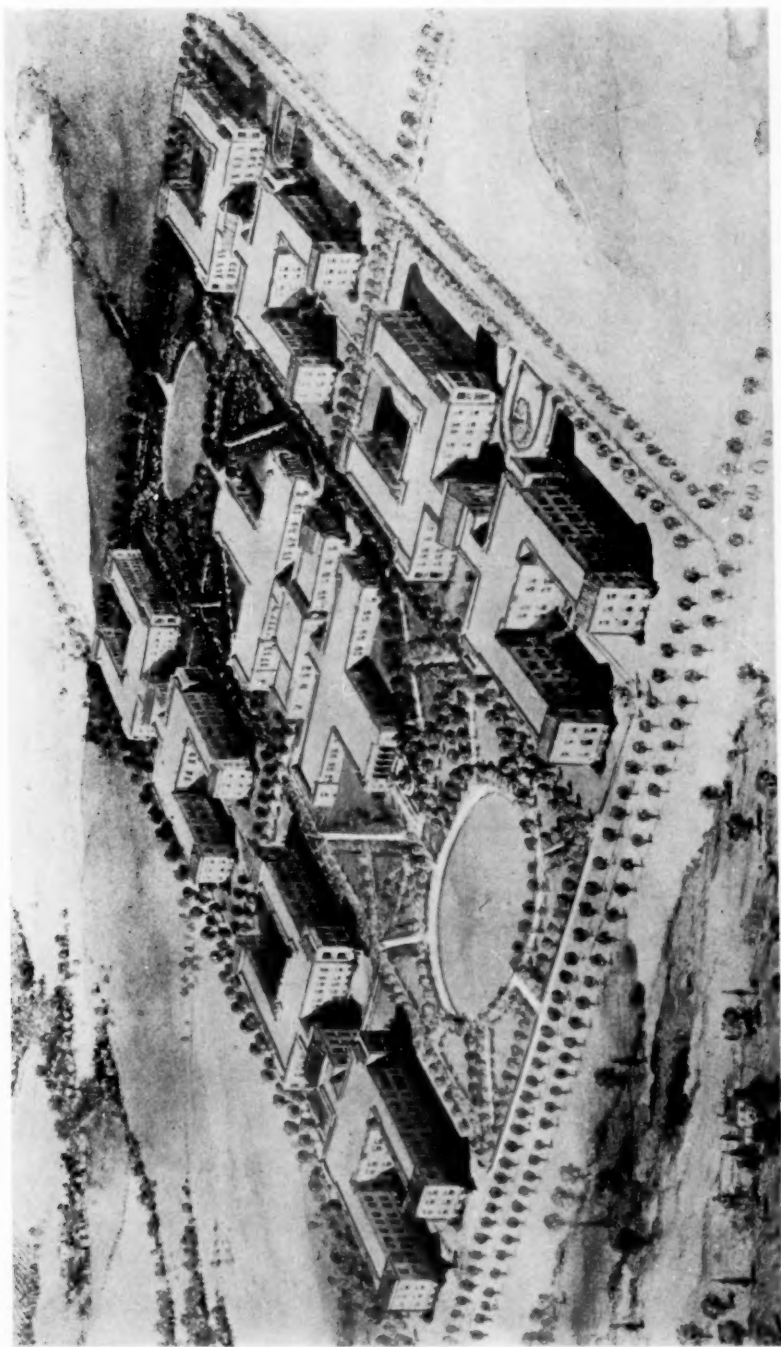
CONTINUED TREATMENT GROUPS

Each continued treatment group comprises four patients' buildings surrounding a central dining room and kitchen. The ward buildings in size and shape are identical but the interiors are modified to provide the facilities needed by patients of various types. In each group there are accommodations for 248 mildly and actively disturbed patients, 416 infirm patients and 816 quiet continued treatment patients. No ward has more than 52 patients and no dormitory more than 10 beds. The wards for the actively disturbed have continuous-flow baths, accommodate 31 patients, 11 of whom have single rooms and 20 patients are in four dormitories, each of five beds. All dormitory capacities are rated on the basis of 50 square feet of floor space for each patient. Three of these groups have been erected and are occupied, the fourth is under contract





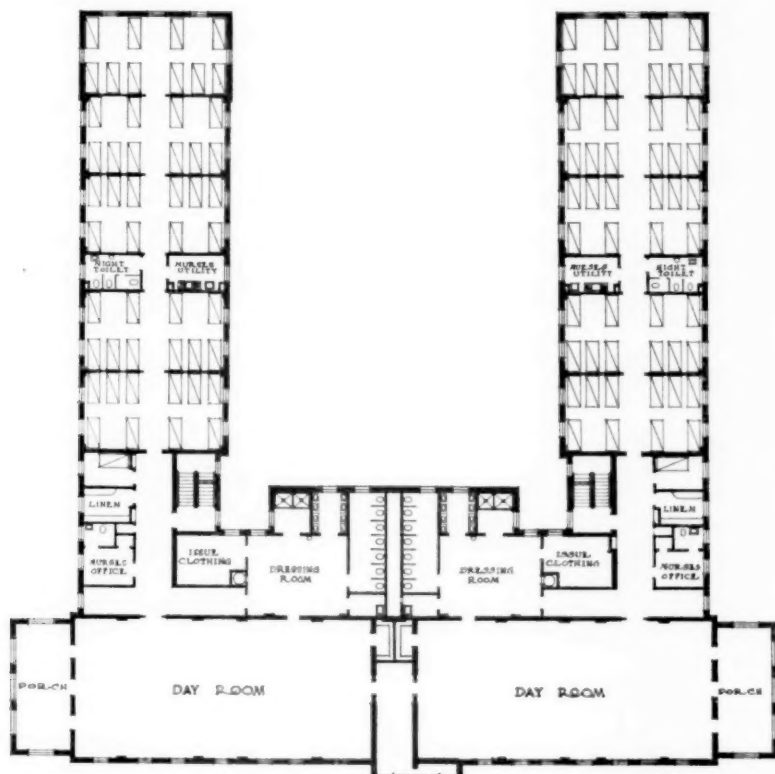
ADMISSION, ACUTE-MEDICAL AND SURGICAL AND DIAGNOSTIC-CENTER GROUP



PERSPECTIVE OF ONE OF THE CONTINUED-TREATMENT GROUPS OF PILGRIM STATE HOSPITAL



and will be completed within a few months. Each group has an occupational therapy center in the dining room building. The plot plan shows a square structure connecting the two halves of each building. Here are provided offices for the physicians, stenographers and supervisors, treatment rooms and accommodations for visitors.



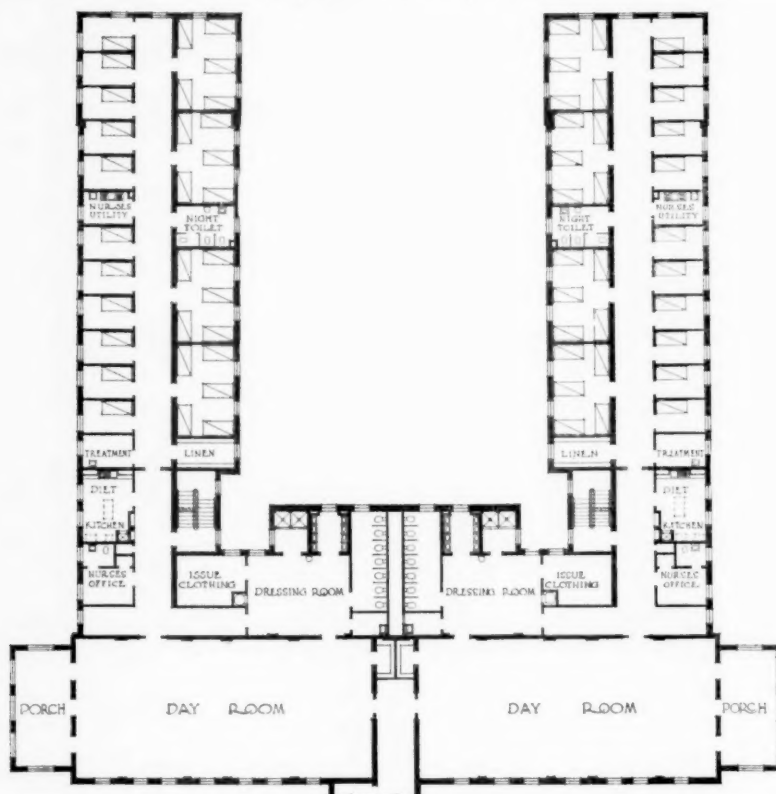
2 TYPICAL WARDS FOR QUIET CONTINUED TREATMENT PATIENTS



INTENSIVE TREATMENT GROUP

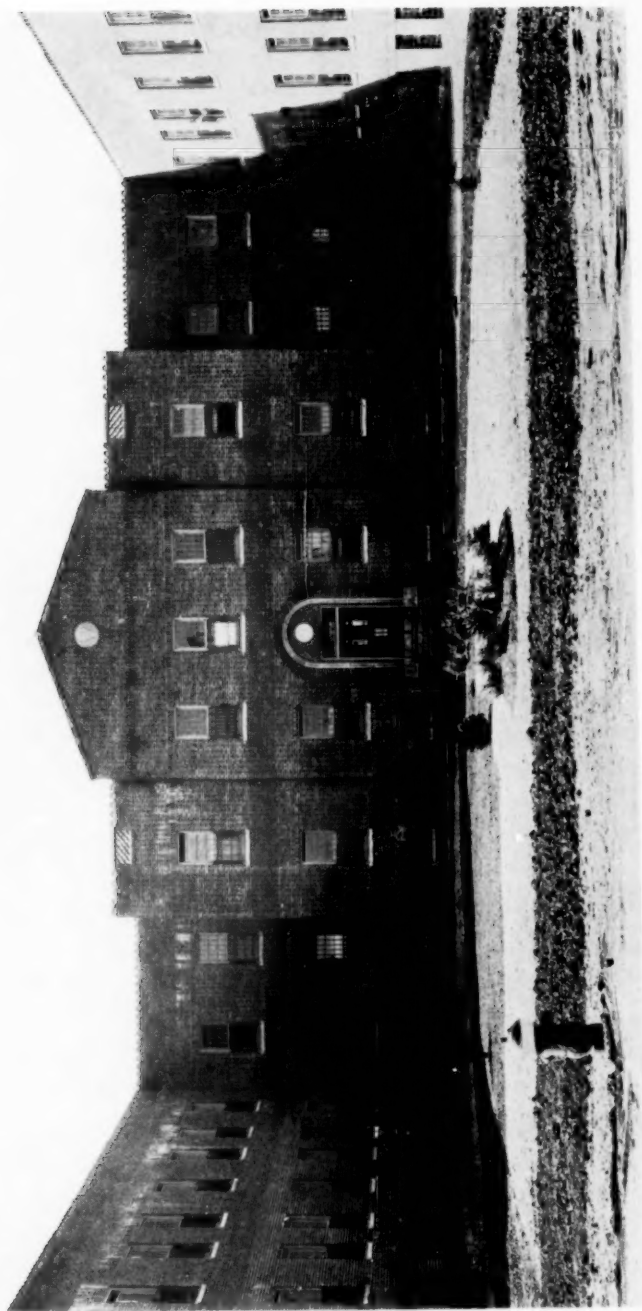
Contracts have been let for the admission—diagnostic center—acute medical and surgical unit, a group of buildings closely related

in work, hence connected by corridors, all being served by one kitchen. The admission building will accommodate 660 patients which provides for an average four months' residence for each patient admitted even when the admission rate is 2,000 patients per year. It is expected that recoverable patients will not leave the admission service for it will have accommodations for patients of all types. The only reason likely to call for the removal of a recoverable patient from the admission building is the existence of tuberculosis or of an acute illness requiring a temporary residence in the general hospital. The diagnostic clinic, available to all patients in



2 TYPICAL WARDS FOR
MODERATELY DISTURBED PATIENTS





ENTRANCE TO A CONTINUED-TREATMENT BUILDING

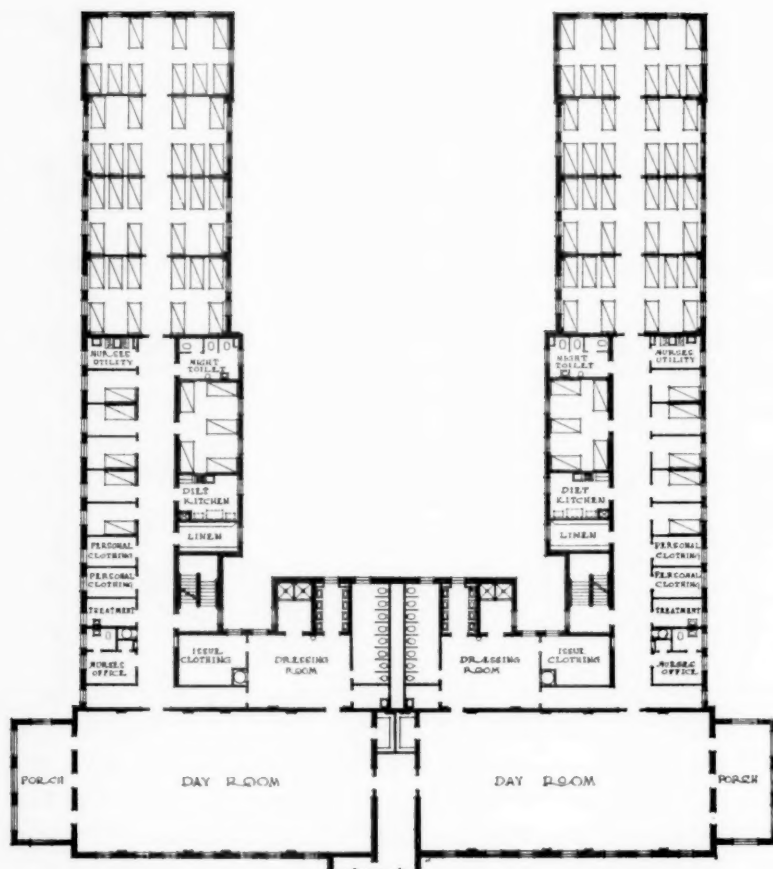
need of special diagnostic facilities and consultation with specialists, is a part of the admission group.

MEDICAL ORGANIZATION

Pilgrim State Hospital will therefore comprise five groups, each under the direction of an assistant superintendent. The first group will be the intensive treatment service which will meet the needs of the entire institution. The other four will be continued treatment groups, each of 1,500 capacity, two for men and two for women. Each continued treatment service has accommodations for all types. This arrangement avoids the stigma which might be attached to a special group of buildings set apart for difficult cases. As each continued treatment group will be a hospital of 1,500 patients, with identical subdivisions of patient population, it will be possible to compare, one group with the other, the number of working patients, the number on parole, the number of patients engaged in occupational therapeutic activities and the accidents and deaths.

The institutional layout includes a utility group, capable of expansion to a 10,000 limit, which at present supplies only the needs of the structures built and building. Pupil and graduate nurses have homes and there are structures both for single and married employees. The staff group, separated a short distance from the institution, furnishes individual quarters for all the physicians. It is proposed to add to this group a staff house for unmarried physicians, each set of quarters to consist of a study, bedroom and bath; and a somewhat similar structure for social workers and occupational therapists. There will be a common dining room for unmarried medical and non-medical officers.

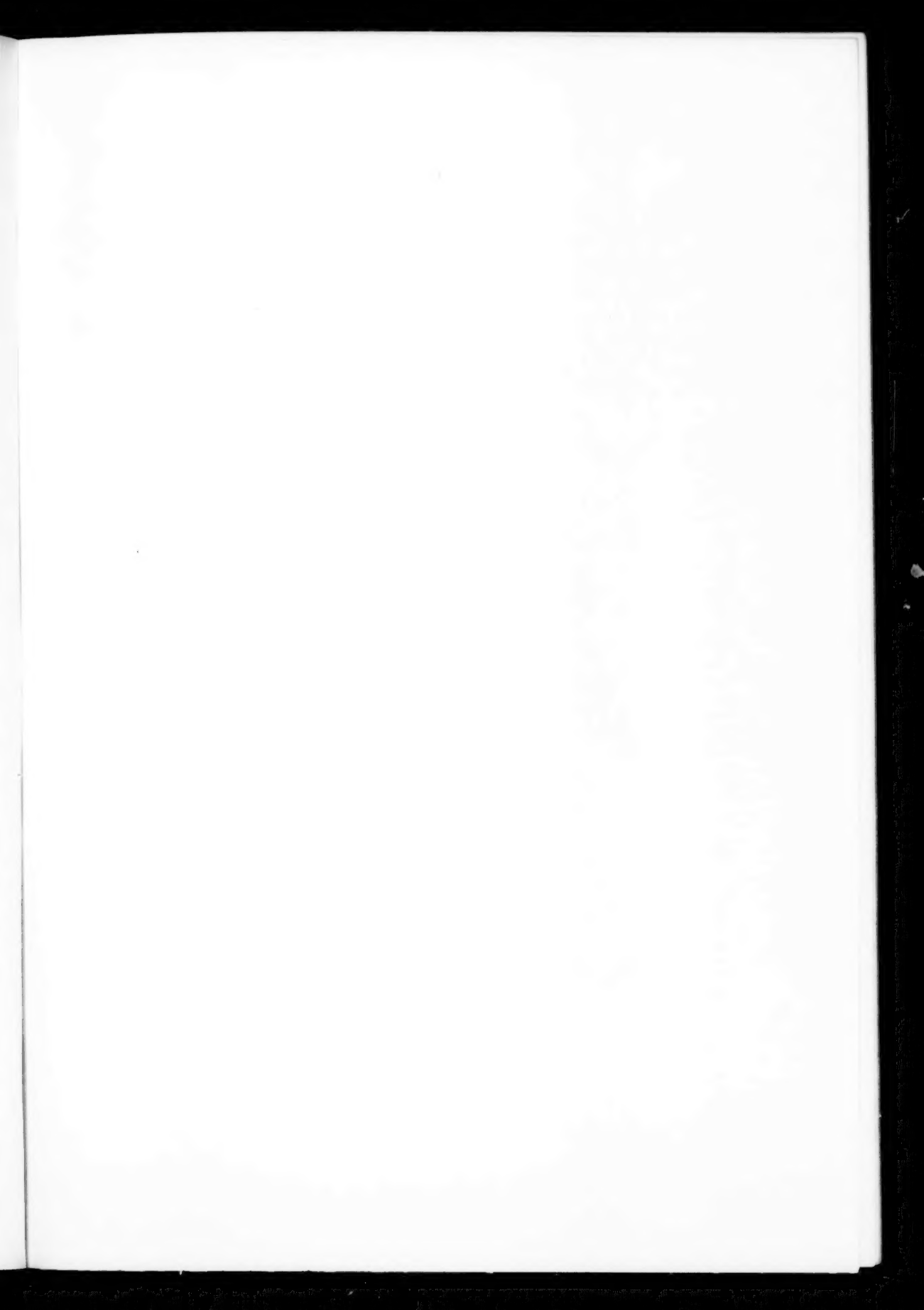
The only additional function which the Department of Mental Hygiene now considers for the Pilgrim State Hospital is accommodations for tuberculous patients. Where these buildings will be located has not as yet been settled but it is thought that structures for such patients shortly will be desirable. As at some of the nearby hospitals frame buildings for the accommodation of tuberculous patients are in need of replacement, the tuberculous group at Pilgrim may be larger than would be required by the admissions and the resident hospital population.



2 TYPICAL WARDS FOR
INFIRM PATIENTS



The Department of Mental Hygiene knows of no reason why a large hospital planned similar to Pilgrim State Hospital cannot effectively function and meet the objections of those opposed to large institutions. In the relatively small continued treatment groups at the Pilgrim State Hospital there should be no occasion for overlooking patients who are making progress towards recovery. The economy of having one power house, one storeroom, one

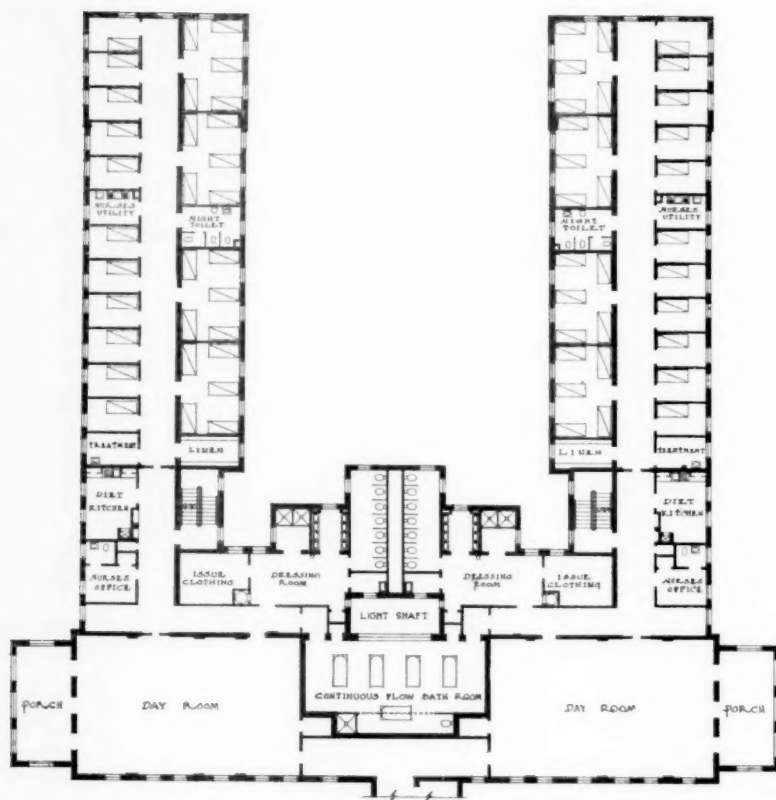




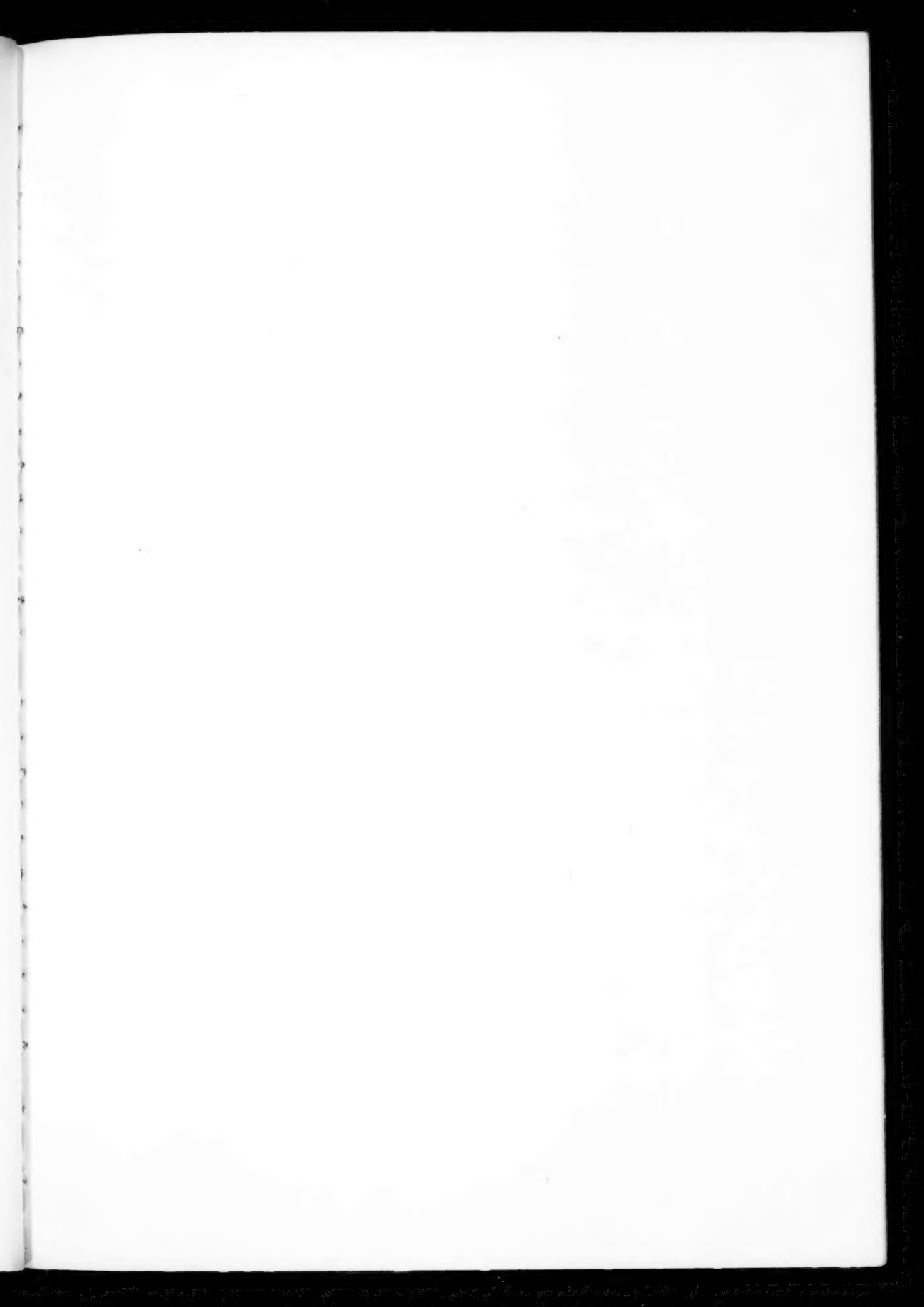
ENTRANCE TO A DINING GROUP

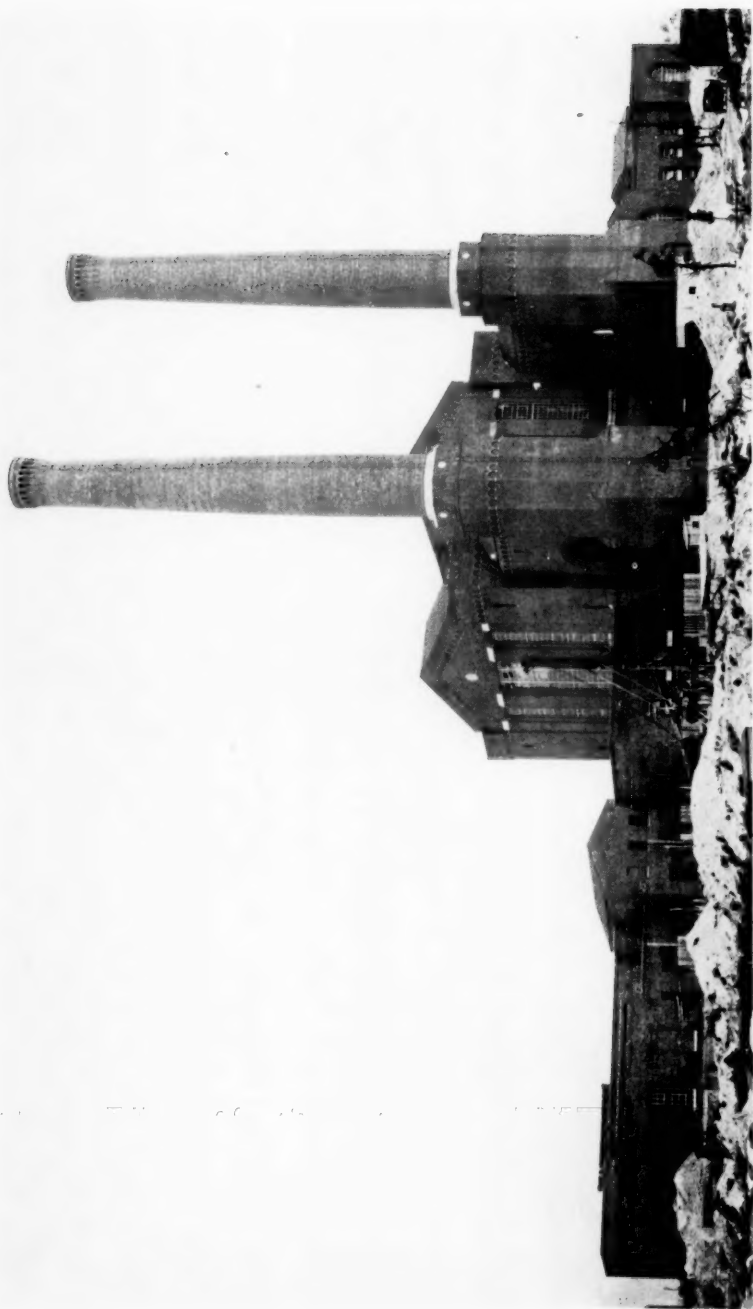
laundry, one water supply and one bakery is apparent. Pilgrim State Hospital will have the advantage of the esprit de corps of a large institution and some if not all of the advantages of the small institution. In this hospital there are but five patient kitchens and cafeteria food service will be widely used. Underground passages permit patients to walk from the ward buildings to the dining rooms and these passages are being used to bring food to wards caring for patients unable to go to dining rooms. On these wards diet kitchens have been provided. Although cafeteria service is in operation the Department of Mental Hygiene is not entirely satisfied with the existing underground passageways. The full benefits of cafeteria service cannot be had unless patients, upon the conclusion of a meal of varied duration, can filter to their wards unescorted. To obtain that desirable end, entrance to and exit from the dining rooms should be by different routes. Then no confusion of traffic is occasioned. The construction of another set of corridors by which the patients can return to the wards would provide ideal conditions although the present confusion is not great and in pleasant weather the patients can go to the dining rooms above ground and return by the corridor route.

The reproductions of photographs, artist's rendering of architect's perspectives and sketches of typical floor plans will show the type of accommodations provided. The continued treatment groups are two-story buildings but the admission group is of three stories. All buildings are of red brick, of concrete flat arch construction with mission tile roofs. The architectural style is Lombardy. Much terrazzo flooring has been used and the structures are fireproof. Cheaper but less durable buildings with greater upkeep cost could have been built but the effort has been to provide first-class construction throughout. The buildings have cost \$19,000,000. Sewage and water supply systems have cost \$1,000,000 and nearly another \$1,000,000 has been spent for the site, the railroad switch and roads, walks and grading. The certified capacity is 6,800 but that allows a sleeping area of 50 square feet per patient which by some will be thought to be over-generous. In reality, to balance the 10-bed wards, 2 additional beds easily can be added. Patient population, 17 per cent in excess of certification, does not appear as over-



The New York State Department of Mental Hygiene does not





POWER HOUSE. VIEW FROM THE REAR PRIOR TO THE CONSTRUCTION OF THE COAL TRESTLE

believe the Pilgrim State Hospital to be a model institution, to be repeated in districts with low admission rates, neither does it think districts should be expanded so that large institutions can be justified. It prefers smaller institutions but when the conditions of a densely populated community make it necessary to provide for large numbers of patients it does not see how huge institutions can be avoided. Pilgrim State Hospital can be considered as four small continued treatment hospitals, which number can be increased if experience indicates that to be desirable, served by a central group of buildings in which every modern hospital facility is available. It is now functioning as a unit of the Department of Mental Hygiene. As this is being written it houses 2,000 patients and by the time the article is printed more than 4,000 patients will be in residence.

The Department is fortunate in having, in Dr. William J. Tiffany, the former superintendent of Kings Park State Hospital, an active, able and experienced hospital administrator who was willing to allow himself to be persuaded to leave an established institution and assume the responsibilities of organizing and directing the Pilgrim State Hospital.

REVIEW OF THE WORK OF THE PSYCHIATRIC INSTITUTE AND HOSPITAL DURING THE PAST YEAR*

BY CLARENCE O. CHENEY, M. D.,
DIRECTOR, NEW YORK STATE PSYCHIATRIC INSTITUTE AND HOSPITAL

It is a pleasure to have the Conference meet here again at the Institute and we are glad of the opportunity of presenting to you facts regarding the activities and interests of the Psychiatric Institute and Hospital during the past year, since the last meeting. The time does not permit of a full discussion of any one particular topic or of detailed mention of all of such activities and interests. More detailed discussions are, or will be, available in the individual papers published by members of the Institute staff or in the annual report.

During the last fiscal year 378 patients were admitted to the hospital, 339 of these being on a voluntary basis. A total of 537 patients was under treatment during the year and 372 were discharged. Fifty-seven per cent of the patients had a residence of less than four months. It is not opportune to discuss the individual diagnostic groupings; suffice it to say that a large majority of patients were cases of general paralysis, of manic-depressive psychosis, of dementia præcox or of psychoneurosis.

During the first five months of the present fiscal year up to November 30, 1932, there were 167 patients admitted to the hospital and 127 discharged.

During the past fiscal year, 5,826 visits were made to the out-patient department, men being somewhat in excess of women. The hospital staff taking part in the activities of the out-patient department continue to be augmented by 12 physicians who are appointed as attending psychiatrists in the out-patient clinic. During the five months of the present fiscal year there have been 1,615 visits made by 303 persons.

During the fiscal year ending June 30, 1932, 45 patients were admitted to the children's service. Their ages ranged from 4 to 16. Eleven of them were under the age of 10, while 34 were 10 years old or over. This age grouping was not a matter of selection on

* Read at the Quarterly Conference held December 10, 1932 at the New York Psychiatric Institute and Hospital.

the basis of age but depended entirely on the need for hospitalization. It may indicate that the majority of psychiatric problems in children below the immediate pre-puberal ages do not require hospital treatment. As a matter of fact it is generally believed that children of younger ages are best treated in their home environments whenever possible.

The cases admitted to the children's service were classified in a variety of diagnostic groupings. The largest number, a total of 19, were classified as psychopathic personalities and psychoneuroses. Nine cases showed a marked emotional instability in association with chronic epidemic encephalitis, mental deficiency, or epilepsy. There were 5 cases of juvenile general paralysis and 7 were diagnosed as dementia præcox. Two cases had a manic-depressive psychosis. One was a case of reading disability and two were behavior problems directly associated with an extremely unfavorable home situation.

Our experience thus far has suggested that psychiatric problems in children, aside from those of organic origin, fall into two groups. One group consists of those cases in which the behavior difficulty is a direct reaction to an unfavorable environmental situation. These children, when the environmental situation is corrected, or when they are removed from it, promptly recover. The other group consists of children in whom there is a large constitutional element, coupled with an unfavorable environment situation. The environmental influences in these cases seem to have invaded the total personality of the patient and these cases continue to be problems, even when they have been removed from the unfavorable environment, or when it has been possible to alleviate the environmental problem. These cases are in need of careful and intensive psychotherapy.

Of the 45 cases admitted to the children's service during the past fiscal year, 23 were discharged during the same fiscal year. The average stay in the hospital for these discharged cases was a period of approximately three months. Two were discharged as recovered, 7 as much improved, 8 as improved and 6 as unimproved. None died. The recovered and much improved discharges were made up of cases with psychoneuroses, psychopathic personalities

and manic-depressive psychoses. The unimproved group consisted largely of juvenile paretics and cases with emotional instability, associated with chronic epidemic encephalitis. During the fiscal year 14 other cases of those admitted during the same year were paroled or have been paroled or discharged since the close of the fiscal year and of these, 8 may be regarded as recovered.

The clinical characteristics of children with dementia præcox and the treatment of such cases continues to be the chief research problem on the children's hospital service. We have been observing that symptoms of dementia præcox occur in children below the age of ten and a number of such cases were reported in detail by Dr. Potter at the meeting of the American Psychiatric Association in Philadelphia in June. There seems to be an interesting difference of opinion among psychiatrists here and abroad regarding the occurrence of dementia præcox at such an early age but our observations here lead us very definitely to believe that this clinical syndrome does appear and it creates problems for investigation and treatment. As with adults, one of the greatest difficulties in the treatment of juvenile dementia præcox is the difficulty in establishing rapport between the physician and the patient. The value of a carefully organized daily routine with school, occupational therapy, gymnastic games, singing, organized play, etc., as methods of objectifying the interests of these cases, is apparent. It has been noted, in all cases of juvenile dementia præcox in which a definite improvement has occurred, that the initial improvement was directly associated with the child becoming interested in some one or another of the daily activities. It might be stated in passing that one of the greatest diagnostic difficulties with this group is the differentiation between dementia præcox and mentally deficient states, especially when a child is under the age of five years.

We are of the opinion that children suffering from dementia præcox may have made the impression, in the past years, of being cases of mental deficiency, particularly if such diagnosis was made on the basis of an intelligence quotient and that these children may have been institutionalized in schools for mental defectives. It appears to us that an inquiry as to the number of juvenile cases of

dementia præcox that might be found in our State schools, would make an interesting and fruitful topic for study.

In the out-patient department, during the fiscal year ending June 30, 1932, there were 250 children admitted, with a total of 1,445 visits. It is almost futile to discuss these cases from a standpoint of diagnosis. The practice of diagnosing many psychiatric conditions as behavior problems appears to have no clinical value whatever. It is interesting to note that so-called behavior problems include a variety of reaction types. A very large number fundamentally have a psychoneurotic basis and careful study of the clinical material offers the suggestion that the fundamental mechanisms are one or another type of psychopathic reactions. Thus in several instances where an extreme quarrelsomeness and inability to adjust to other children is found, there appears to be an incipient paranoid reaction.

During the five months ending November 30, 1932, 45 children were admitted to the hospital, a number identical with that for the entire previous fiscal year.

In our review presented last year at the Quarterly Conference, we indicated that we had begun an investigation of oxygen and carbon dioxide treatment of patients showing dementia præcox reactions, it having been previously noted by some investigators that there was evidence that cases of dementia præcox had a deficient oxygenation, and that possibly, if a normal supply of oxygen should be supplied to the patients, particularly to the nervous system, more adequate mental functioning might result. We reported last year that an oxygen chamber had been used and that following a period of approximately two months' living in the chamber with 50 per cent oxygen and with daily inhalations of 12 to 15 per cent of carbon dioxide, certain patients had seemed to show some improvement during and subsequent to the treatment. We indicated at that time that, because of psychological factors involved, we did not then feel able to evaluate the changes that seemed to have taken place.

Through the continued generous cooperation of Dr. Alvin L. Barach of the Presbyterian Hospital, who was instrumental in procuring for us the services of a technician and the necessary ap-

paratus as well as the oxygen and carbon dioxide without cost to the hospital, we were enabled, during the past year to extend an investigation of this form of treatment. A dormitory on one of the wards was remodeled into an oxygen chamber to care for 10 male patients showing the catatonic form of dementia præcox. These patients, from March 15 to June 10 resided continuously in this chamber, sleeping and having their meals there. Five of them received only the treatment of 50 per cent oxygen with 3 per cent carbon dioxide which was constantly supplied as an atmosphere. Five of the patients in the chamber received in addition, daily treatments of carbon dioxide varying from 15 to 20 per cent to 40 per cent for one or two minutes a day. Five other male patients showing the catatonic form of dementia præcox who were on the same ward but not in the oxygen chamber, received daily treatments of carbon dioxide. Blood studies were made of these patients before and during treatment. Our observations did not confirm previous reports of other investigators regarding the evidence of deficiency of oxygen in the blood of dementia præcox patients but on the other hand, showed that the blood oxygen content was within normal limits and that there was no appreciable change in the oxygen content under treatment. This group of 15 patients, both those in the oxygen chamber and those receiving carbon dioxide treatment on the ward, showed no appreciable clinical improvement during the period and we thus feel that we are in a position to say that the investigation that we have carried out does not indicate that the catatonic form of dementia præcox can be definitely relieved by this method of oxygen and carbon-dioxide treatment. The method has been discontinued and we feel that we are in a position at the present time not to advocate the installation of oxygen chambers in the various hospitals. Our feeling regarding the treatment with carbon dioxide is that although it may result temporarily in a removal of the stuporous reaction, in other types of the catatonic form of dementia præcox it does not seem to have a definitely beneficial effect except that it may bring about communicativeness in the way of protests from patients because of its disagreeable and somewhat terrifying nature.

A review of the histories of two patients in the first small group

who improved sufficiently after treatment to be able to leave the hospital, indicates that they were of the type of reaction from which improvement or recovery might be expected because of their previous comparatively good adjustments, short duration of symptoms and the type of symptoms. The details of the work will be published later.

Because of our special interest in the catatonic form of dementia præcox, this type of disorder was chosen as the subject for a symposium for interhospital conferences here at the Institute and at the Utica State Hospital, in April, 1932. At that time contributions were made by the Institute staff and by members of the various hospital staffs which we feel have been well worth while. A number of these contributions have already been made available to the members of the conference by having been published in the *PSYCHIATRIC QUARTERLY*.

We might emphasize the point brought out by this symposium confirming other observations, that as one studies a large series of dementia præcox patients, a fair proportion of them gain and maintain a so-called adequate type of adjustment, quite apart, as far as is known at the present time, from the nature of the onset or from the duration of symptoms or from the depth of the regression. One tends to be led away therefore, from a fatalistic attitude in the diagnosis of dementia præcox, particularly of the catatonic form.

The studies carried out by the department of psychology under the direction of Dr. Carney Landis, research associate, on sleep postures of catatonic dementia præcox patients have been, we have felt, of distinct interest.

By special arrangement of equipment it was possible to photograph postural changes of these patients during sleep at night and it was ascertained that in general, those patients who showed catatonic manifestations when awake, assumed normal positions during sleep and changed these as frequently as normal persons, tending, we believe, to show that the postural rigidities of catatonic dementia præcox are of cerebral and possibly of psychic origin rather than determined by toxins as some observers have been inclined to advocate.

The work of the department of neuropathology under the direction of Dr. Ferraro, with bulbo-capnine injections in monkeys and cats and with experimental lesions of the brains of these animals showed that the condition of catalepsy could be produced in animals even after removal of the entire cortex, disproving the contention of those who believe in the cortical origin of this manifestation brought about by bulbo-capnine. It was found that with bulbo-capnine intoxication we presumably are dealing with a diffuse toxic substance which may even act as peripherally as the muscular structures themselves.

Another problem of special interest to us during the past year has been the high frequency field treatment of cases of general paralysis which was begun in July, 1930. By January, 1932, 68 cases had been treated. The method of treatment and the results in these cases were reported in detail by Dr. Hinsie and Dr. Blalock previously (April, 1932, number of the *PSYCHIATRIC QUARTERLY*). At that time remissions were shown by 12 patients, improvement by 24 patients, with 6 deaths. This group is still being followed and it will be of interest to determine the results in another year. Since January 1, 1932, 30 additional patients have completed high frequency field treatment, so that the total number of cases treated at the present time is 98. Beginning July 1 patients who had completed their treatment six months previously and new cases, immediately following the treatment, were placed on a course of tryparamide. It is too early at the present time to draw final conclusions about this whole group.

An instance of the possible application of animal experimentation to clinical psychiatry is indicated in the following: It has recently been called to our attention that Lebedewa and Galanowa in investigating relapsing fever inoculated into mice, showed that heating the mice to 40° C before inoculation and after inoculation seemed to result in brain sterilization or freedom from the spirochaete of relapsing fever, as compared with the continuation of the organism in animals that were not so heated, and also that the brains of heated mice showed 5 to 10 times more arsenic after arsenical injection than did the brains of mice that had not been so heated. This would seem to indicate, possibly, better penetration

and diffusion of arsenicals in association with the production of fever. We plan, therefore, to treat cases of general paralysis with high frequency field treatment and tryparsamide simultaneously to investigate this matter of the combination of fever and arsenical treatment at the same time.

Three hundred and ninety-two high frequency field treatments were given during the last fiscal year. It may be of interest to note at the same time that in the department of physical therapy there were given a total of 23,500 treatments or approximately 2,000 a month. These treatments include applications of the ultra-violet ray, hydrotherapy, diathermy, phototherapy, Morse wave, and massage as well as high frequency field treatment.

During the past year a special investigation was carried out on the effects of the administration of sodium amytal and sodium rhodanate, the latter drug being used particularly in view of Bancroft's reports of the beneficial effects in certain types of cases and the apparent opposite effects of sodium amytal and sodium rhodanate. Seventeen women patients were selected for this comparative study. The results were reported by Dr. Harris, research associate in internal medicine and by Dr. Katz, senior psychiatrist of the Institute staff, at the meeting of the American Psychiatric Association in Philadelphia in June. The complete paper will be published in the American Journal of Psychiatry. The conclusions arrived at were:

1. Sodium amytal, intravenously, may produce marked transient ameliorating effects in some psychotic patients.
2. The temporary improvement with sodium amytal seen in some cases occurred without the induction of narcosis.
3. The oral administration of sodium amytal, even in hypnotic doses, was not as effective as the intravenous in producing the transient ameliorating manifestations seen in some of the patients.
4. Sodium rhodanate was without any noticeable therapeutic effect in the cases studied.
5. Some toxic manifestations were observed in several cases following the oral administration of sodium rhodanate.
6. No contrasting effects were observed between sodium amytal and sodium rhodanate which could be of diagnostic value.

We do not feel that we are as yet in a position to know the exact effect of these drugs on the central nervous system and we are not of the opinion that the clinical effect of these drugs are proven to be manifestations of the direct effect of the drugs on the nerve cell colloids.

The occurrence of psychoses in relation to puberty, menstrual cycles and the menopause has suggested the possible importance in the pathogenesis of some psychoses of the pituitary gland, which seems to be the driving force for growth and the sex cycle. Through the kindness of the Parke, Davis Company, a preparation called antuitrin-S was obtained with which a clinical study is in progress on the women's service by Drs. Harris, Katz and Horwitz. Twenty-eight patients presenting various clinical pictures such as involutional melancholia, manic-depression, schizophrenia, benign stupor with amenorrhea and hypopituitarism have thus far been studied over a prolonged period. An appreciable number of the patients have improved clinically during the period of treatment. It is as yet difficult to say whether the results obtained were merely coincidental or due to the treatment. For example, one of the patients who has been ill for about twelve years and who had received psychotherapy, stated, for several months during a period of hormone treatment, that she had never felt as well in the past twelve years. Recently, with the loss of her position and the resulting financial stress, this patient has grown worse and the hormone has failed to produce any ameliorating effect at this time. Another patient with involutional melancholia stated, the day following the injection, that she felt as if a load had been taken off her shoulders. Other patients with dramatic ameliorating effects have been observed but as indicated previously one must be cautious in crediting the therapy for the changes observed.

In some patients with symptoms of premenstrual nervousness, administration of the hormone has been accompanied by marked diminution or disappearance of some of the symptoms.

A number of patients with amenorrhea have had a return of menses which has been accompanied by either no change in the psychotic manifestations or an amelioration. No aggravation of symptoms has been observed. This investigation will be continued.

In the department of bacteriology, under the direction of Dr. Kopeloff, during the past year it has been possible to successfully bring to a conclusion several interesting problems while others are still in progress. Through the kind cooperation of the various State hospitals we have been able to follow the continuous human passage of a sexual strain of malaria inoculated in patients with general paralysis to the point where all sexual forms entirely disappear from the stained blood smears; approximately two and one-half years were required to obtain this true biological adaptation of the malarial parasite. The advantages of a completely asexual strain are that it precludes the possibility of the accidental transmission of malaria by the mosquito; there is less danger of a recurrence of malaria in an inoculated patient; and asexual malaria yields more readily to quinine than do sexual forms.

This work was carefully controlled by simultaneously comparing the Institute strain of malaria which is asexual, with the Poughkeepsie strain which had sexual forms in the beginning.

A histological study has been made of the brain sections of the malarial treated and untreated general paralytics for the presence or absence of *Spirocheta pallida*. While this work is not yet complete it would appear that in only a very low percentage of malaria treated cases is *Spirocheta pallida* to be found whereas in 80 per cent of the untreated cases of general paralysis were spirochaetes found. Attempts at the artificial cultivation of the malarial parasite have failed thus far, in spite of the variety of methods used in attacking this problem, e. g., thyroidectomy, parathyroidectomy and pancreatectomy in rats, as well as attempting to lower their resistance by large doses of benzene and typhoid vaccine, etc.

The high frequency field was used for treating experimental herpes encephalitis in rabbits but it was not possible to raise the body heat to a point where it would kill the virus and not the animals.

Some years ago, Dr. Brand, research associate in biochemistry and Dr. Harris, research associate in internal medicine, worked at Montefiore Hospital with patients suffering from pseudo-hypertrophic muscular dystrophy. The outcome of this work was the new

and important finding that glycine, the most simple amino acid, had to be considered as the substance from which creatine is formed. Creatine itself is very important in muscular physiology because in combination with phosphoric acid, it is probably the substance which is responsible for muscular contraction. During a muscular contraction, creatine-phosphoric acid is split into its constituents, creatine and phosphoric acid, and during the relaxation, these two constituents combine again to creatine-phosphoric acid. This process goes back and forth, apparently indefinitely. It was therefore an important finding that glycine was the mother substance of creatine. When Dr. Brand and Dr. Harris left Montefiore Hospital, they did not pursue this work further but Prof. Thomas of Leipzig, who for many years has been identified with work on creatine was informed of the work and its results.

Thomas and Milhorat soon began work in Leipzig with patients suffering from muscular dystrophy and fed them glycine for three months and longer. Thomas found that some cases of muscular dystrophy were markedly improved by prolonged glycine administration.

Dr. Harris and Dr. Brand this year resumed their interest in their previous work. A grant of \$2,500.00 from the Chemical Foundation to the Institute was made for investigating the problem. A circular letter was written to a number of prominent clinicians, heads of departments of medicine, and biochemists of various medical schools. Some of these men have started work on the problem and are communicating their results and exchanging ideas.

With full cooperation of the Neurological Institute and others, especially the commissioner of health of Westchester County, Dr. Nicoll, approximately 50 patients have been investigated, of which number about 12 received glycine treatment. None of the cases that have received glycine treatment has shown any definite clinical improvement, contrary to the statement of the German authors. However, a number of interesting observations have been made which are still under investigation in regard to their therapeutic value.

There are statements that cases of myasthenia gravis are supposed to be improved by the glycine treatment.

We also expect to initiate experimental glycine therapy in some psychiatric patients who show definite muscular involvement.

During the past ten weeks the Institute staff has been actively engaged in participating in the post-graduate course in neurology and psychiatry which was completed yesterday. Sixteen men from the State schools and State hospitals attended the course, with, in addition, four physicians not connected with the Department. We feel that the modifications made this year in the course have resulted in some improvement and we shall be glad to consider suggestions for further improvement from the superintendents of the institutions in the Department when they receive such suggestions from the members of their staffs who have taken the course.

We have tried to indicate in this communication some of the problems on which we are working and shall feel gratified if this report of our work shall have proved of some interest to the members of the conference.

FAMILY CARE AND THE INSTITUTION PROBLEM*

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MENTAL HYGIENE

The expansion of institutional care of mental patients in this State during the past decade is a social development of great import. From July 1, 1922 to June 30, 1932, the resident patients in New York civil State hospitals increased from 37,713 to 52,364, an addition of 14,561, or 38.8 per cent. This increase of 10 years is practically equal to that of the preceding 20 years. Due to the efforts of the State to relieve overcrowding the growth of our hospital plants during this period is still more impressive. The expenditures for new construction and permanent betterments in civil State hospitals during the past decade were over \$92,000,000. Like expenditures from the beginning of State care of the insane in 1836 down to 1922 were about \$42,000,000.

Increases in mental patients are cumulative and the annual ratio of increase is gradually rising. We are hoping for a change of trend, but if such change does not come, the next generation will be troubled by an enormous institutional problem. Our present problem will look small in comparison.

Is there no way of escape from the heavy institutional burden that is now upon us and is getting more oppressive year by year? Our thoughts naturally turn to the possibility of prevention of mental disease. We should all agree that prevention would be a happy solution. With the development of mental hygiene and other preventive measures we have been hoping that mental disease would gradually decline and that the number of persons requiring admission to our hospitals would accordingly decrease. Our hopes have not been fulfilled and we cannot expect their fulfillment in the present generation.

In considering the matter of prevention it must be remembered that research in this field is comparatively new, and that the principles thus far developed have not been extensively applied. If research is continued and if the public generally can be persuaded

* Read at Quarterly Conference at Psychiatric Institute and Hospital, December 10, 1932.

to adopt available means of prevention, there can be no doubt that many mental disorders will gradually decline.

Curative treatment presents another possible avenue of escape from the institution burden. If we could speedily cure dementia præcox, for example, nearly half of our mental patients could be discharged. We know not what the coming days may bring forth in the way of therapeutic measures but the present trend in recovery rates does not afford a basis for untempered optimism. The gratifying gain made in recent years in the treatment of general paralysis affords great encouragement to research workers and gives a basis for the hope that other important curative measures may be forthcoming.

Judging from data at hand our institution population seems certain to increase in spite of all of our efforts to prevent or cure mental disease. This being the case, we have to consider whether we should continue to build new hospitals for the care of all of the patients desiring treatment or whether a more economical and more natural method of care may be found for a portion of them.

At present we allow a large number of unrecovered patients to go into the community on parole or trial visit. If these patients adjust properly to community life, they are eventually discharged. If they do not adjust they are returned to the hospital. The family care of patients which I am presenting for your consideration this morning is merely an expansion and extension of such parole system. The principal distinction between family care and parole as now practiced lies in the matter of support. Paroled patients are usually placed with relatives or friends who agree to become responsible for the patient's maintenance; under the family care system the State or other public authority pays wholly or in part for the care of patients in private homes, usually homes of persons who are strangers to the patients.

The classic example of successful family care of patients is the well-known Colony of Gheel in Belgium. This Colony has such a unique character and such an interesting story that it has become familiar to nearly everyone interested in the care of mental patients. The district about Gheel in which the family care of patients has probably reached the most satisfactory stage of develop-

ment, comprises about 300 square miles and had about 18,000 inhabitants. The village of Gheel constitutes the social and industrial center of this community. Here is the shrine of Saint Dymphna to which mental patients used to come and here is a small hospital that accommodates about 100 mental patients. This serves as a reception and distributing clinic for the family care system of the community. A director serves as head of the hospital and manager of the system of family care. He is assisted by five psychiatrists and by a number of nurses who work under the direction of the assistant physicians. The Colony is supported by the Kingdom of Belgium but patients who can afford to pay for their care are required to do so. A patient coming to the Colony is received in the central hospital. If he is deemed suitable for care in the Colony he is kept in the hospital a few days and is then placed out in one of the private homes authorized to receive patients. The placement of patients is conducted by a permanent committee which consists of the burgomaster of Gheel, one alderman, three members appointed by the Minister of Justice of Belgium and three physicians attached to the Colony. It seems probable that the medical members control in large measure the action of the committee. In most cases a home satisfactory to the patient and his relatives is found and a definite rate for maintenance is fixed.

The homes differ widely in the accommodations they afford for patients' care. The rate of pay also varies greatly. It may run anywhere from \$30 a year to \$500 a year. The latter amount is paid only by patients of large means. The families who take patients have acquired a high degree of skill in managing mental cases and it is said that in most instances patients are happy and contented and adapt well to the routine of family life. Patients who are able to work may be employed on the farms or in the gardens of their caretakers or they may work at various trades. They are not coerced but are persuaded by gentle means to lead active, useful lives. They are not confined to the home of the caretaker but may go about the district at will. They must return to their homes early in the evening.

Throughout the whole Colony there is a friendly, sympathetic

attitude toward patients so that help is available for any patient who gets lost or who becomes ill while away from home.

The continued success of this Colony is due principally to able medical direction and to the ability to manage patients acquired by the people of the Colony during a long period of years. The latter now regard the care of patients as an important part of their business and community life, and derive much satisfaction from the service rendered. The peace and contentment of neither family nor community life are greatly affected by the presence of the patients.

A different type of family care is found in Scotland. In such country, a supervised system of family care of mental patients was authorized by an act regulating the care and treatment of lunatics passed August 25, 1857. This law was the outcome of an investigation made in 1855 by a Royal Commission appointed to inquire into the "State of Lunatics and Lunatic Asylums in Scotland. The report of the Commission stated that there were in Scotland 2,839 patients in public institutions, including 8 asylums, and 12 poorhouses with separate wards for the insane; 657 patients in private establishments; and 1,363 in private houses. All types of care then in use were deemed unsatisfactory. The commissioners urged district boards to build new asylums and to license private homes, each to care for not more than four patients. The following is an abstract from their report:

"That all cases of insanity should be placed in an asylum is a proposition we cannot entertain; the welfare of the patients would not thereby be promoted, while the expense to the country would undoubtedly be greatly increased * * * * All great aggregations of permanently diseased minds are evils which should, as much as possible, be avoided, as their tendency is undoubtedly to lower and degrade each constituent member of the mass. Viewed in a certain light, then, asylums may be regarded as necessary evils; * * * * we would gladly see enacted, that any number of patients, not exceeding four, might be received into a private house * * * * Under some such provision we feel satisfied that a system of cottage accommodation would gradually spring up, which would not only furnish more fitting accommodation for chronic patients than the lunatic wards of poorhouses, but would also be calculated to prove a valu-

able adjunct to asylums * * * * The practical advantages of such a system would be, the greater amount of liberty accorded to the patients; their more domestic treatment; and their more thoroughly recognized individuality."

The recommendations of the commissioners were put into effect by a law which, in the main, is still in force.

An article by Dr. George Gibson, Deputy Commissioner of the General Board of Control of Scotland, published in the *Journal of Mental Science* for April, 1925, states that the number of patients in licensed houses gradually increased down to 1913 when it was 2,909. The number was reduced during the World War. In 1925, it was 1,789. His views of the scope and value of family care are seen in the following quotation from his paper:

"For practical purposes patients might be regarded as belonging to two classes, those who are going to improve and those who will never get any better. As long as there is any chance of recovery we should neglect no methods which may result in curing the patient. Let us be as scientific and as modern in our methods as is possible. But when no improvement is possible, when the case is chronic and will be so until the patient dies, are not kindness, gentleness and the maximum of freedom of greater value than all the psychoanalysis and bacteriology in the world? I would humbly submit that those are to be found in making the patients' surroundings as much like home as possible, and would venture to suggest that this more cheerful home-life is to be found rather in the private dwellings and specially licensed houses of Scotland than in the wards and day-rooms of our asylums."

The system of family care in Scotland differs from that at Gheel in that there is no close grouping of cases in localities, and less intimate medical supervision. In the former, local authorities may place a patient in a licensed house whenever they deem it advisable to do so; or a patient may be transferred from a hospital to a private home. Paroled cases that cannot independently adjust to community life may also be sent to private homes.

As would be expected, the family care of patients is economically managed in Scotland. It was stated a few years ago that some patients were boarded for as low as 50 cents per week and some for as high as \$2.00. Probably higher rates prevail at the present time.

In the Canton of Zürich, Switzerland, family care of the insane was begun in April, 1909. Patients were placed in country homes with the hope that life on the farm would be beneficial to them. At the start, quiet types of the mentally diseased and mentally defective from the hospital at Rheinau were placed with farmers in the neighboring village and the surrounding country. In the first year 100 patients were thus placed. The number increased up to 1914. For several years thereafter the number decreased, both patients and farmers becoming dissatisfied with the financial arrangements. By 1919, these conditions had been overcome and the number of patients placed in private families again increased. The family with whom each patient is boarded receives a small allowance paid by the patient when possible or paid jointly by his commune and the Canton of Zürich. Some families, however, make no charge for the care of patients and in a few cases patients receive pay in addition to maintenance for their work on the farm of the caretaker. Many families care for two or more patients.

For several years past the family care of patients in the Canton has been under the direction of the Burghölzli Hospital of which Dr. Eugene Bleuler was formerly director. The present director, Dr. Hans W. Maier, is also well known to American psychiatrists. The latter in a recent letter to the writer states that the results of the placing-out system are very satisfactory. His hospital has a special board for inspection of the homes of families caring for patients. The medical supervision of the patients placed out is conducted by an assistant physician of the hospital. Dr. Maier states that the patients under family care are suffering from chronic mental disease and have improved so that the hospital treatment is no longer needed, but, on the other hand, they cannot live in full liberty in the community and do not have families of their own to care for them.

At the present time nearly 400 patients from this hospital are being cared for in families. In 1931, the new cases placed out numbered 68, of which 36 were males and 32 females. Thirty-five males and 39 females were discharged from family care during the year.

In Germany, family care of mental patients is in use to a consid-

erable extent in several localities. The system has been most extensively developed by Dr. Gustav Kolb, superintendent of the hospital for mental patients at Erlangen near Nuremberg. Using his hospital as a center, Dr. Kolb is boarding out in private homes in the surrounding country a large number of patients who otherwise would be institution cases. According to the latest data available, he has now under supervision in homes about 4,000 patients although his hospital accommodates only about 1,000. The plan of care and supervision is very similar to that in use in the Canton of Zürich, Switzerland.

When Dr. Kolb began the placing out of patients in 1911, he found it a difficult task. Many homes were canvassed before suitable places for six dementia præcox patients could be found. The experience of the families with these patients proved so satisfactory that requests from other homes for patients soon came to the hospital. The patients also did well in their new homes. From that time on, with the exception of the war period, the system has expanded and other hospitals have profited from Dr. Kolb's experience.

Family care for remuneration, or the boarding-out system, has not been widely used for mentally-ill patients in the United States. In the State of New York we have no record of its official use at any time. The State of Massachusetts, however, has for many years, boarded out a limited number of patients. In 1889, Dr. Henry R. Stedman made a comprehensive report of the condition of the boarded-out insane in such state. He personally visited nearly all of the cases placed in families and made careful records of his observations. The homes in which he found patients were classified in four groups two of which were found satisfactory. The other two groups were inadequate and unsuited for the purpose. In summing up his lengthy report he submits the following conclusions:

"1. The defects in the operation of this means of provision for the chronic insane in Massachusetts have been largely due to the difficulties inseparable from the introduction of any new and extended system of public charity.

"2. As regards good guardianship and care, a more natural life, increased comfort to the insane who enjoy its privileges, and

economy to the State, this method of caring for the insane has been in the main a successful provision but for a relatively small number of patients. Until, however, it has stood a longer test, it cannot be said to have passed the experimental stage, and only when it has become a thoroughly organized institution with fully developed resources can it be pronounced an established success.

"3. As a means of relief to the lunatic hospitals from overcrowding the value of this method is at present inconsiderable.

"4. Under the present restrictions it serves as a useful, humane and economical accessory provision for the insane, which may ultimately take rank with the lunatic hospitals, in point of numbers cared for, thereby precluding the necessity of constructing other accommodations for the insane.

"5. Should the town authorities generally throughout the State consent to the transfer to family care of their charges in the lunatic hospitals, who are suitable cases for such outside care, the family system, rightly conducted, cannot fail to be a valuable means of delaying the over-accumulation of the insane in the hospitals.

Notwithstanding the possibilities set forth by Dr. Stedman, the boarding-out system in Massachusetts has never reached large proportions but has been continued for a relatively small number of patients down to the present time. During the fiscal year which ended November 30, 1930, 82 cases were placed in family care. The number remaining in such care at the end of the fiscal year was 169. For the patients placed directly by the Department of Mental Diseases the weekly cost in such year was \$6.22, of which \$4.15 was paid for board and clothing.

Whether it would be wise to extend the present parole system in this State by placing patients in families as is being done in Massachusetts, Gheel, Germany, Scotland, Switzerland and some other countries is a question which deserves full consideration. If the following questions can be answered in the affirmative it would appear that a system of family care should be undertaken in this State:

1. Would patients be as well cared for in family homes as in institutions?

2. Could family care be made satisfactory from a psychiatric viewpoint?

3. Could mental patients be placed in homes so that no harm would come to the home in which they are received or to the community in which they are placed?

4. Would the cost of family care to the State or to patients who can afford to pay be less than that of institution care?

5. Would a considerable number of suitable homes in several parts of the State be available for mental patients?

6. Could a community system of care such as prevails at Gheel be developed in villages in this country?

While it seems probable that an affirmative answer could be made to all of these questions, the matter would be positively determined only by trial demonstration. It is thought that within easy reach of the present State hospitals there are several villages that would constitute favorable centers for family care. There should also be available many former State hospital employees, who now maintain homes of their own that would be willing to care for patients therein.

Having in mind the great institutional problem before us and the experience of other countries, I believe that family care of mental patients deserves the serious consideration of the authorities of this State and that a trial demonstration under as favorable circumstances as possible should be made.

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PSYCHOSES IN IDENTICAL TWINS

A Contribution to the Study of the Etiology of Functional Psychoses

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Before the recent development of the classification of the psychoses into its present, generally accepted, form, mental disorders were differentiated on a relatively uninvestigated basis and according to symptoms and prognosis. With the differentiation of the various organic types and the establishment of their clinical and pathological entities, the remaining types took on an appearance of more definitely functional character, the large fund of data which had accumulated having failed to demonstrate an organic basis. A vast clinical experience has been correlated with extensive laboratory observations, many data having been gathered and analyzed by competent and conservative investigators, but, although advantage has been taken of the known resources of medical science, an organic basis for these mental disturbances has not been proved. In dementia præcox, for example, post-mortem histological investigations have led some observers, such as Mott, to declare with some degree of assurance that changes have been found, in the cells of the cortex especially, which were sufficiently uniform and of such nature as to be regarded as characteristic of the organic nature of the disease process. Others, such as Dunlap, after having carefully checked these observations, and found similar changes in other brains, have concluded that such claims were not warranted.

At the same time, certain psychiatrists, notably Meyer in this country, recognizing the possibility of these mental phenomena being dependent upon mental activity alone, pursued their studies along these lines and evolved a theory of a psychobiological basis, in which it is postulated that the subject's mental equipment, without organic impairment, reacts to life experiences and problems in an immature, insufficient or unsuccessful manner, the psychosis resulting as a compromise solution of the difficulties.

Psychoanalysis, receiving its greatest stimulus from Freud's

conception, which some critics find unduly generalized in its sexual themes but which in formulations is none the less revealing and indicative of mental mechanisms, developed a psychological conception of the so-called functional psychoses and psychoneuroses. We now have an extensive accumulation of data, from which have been drawn well substantiated conclusions as to the phenomena of normal mental development, previously unrecognized, and as to the manner in which abnormal mechanisms deviate from healthy ways of thinking.

It was observed, particularly by Hoch, that in persons with schizophrenic mental disorders, there is a preponderance of a particular type of personality, and in those affected with a manic-depressive psychosis, a preponderance of another particular type. It was therefore believed that the soil on which these special mental aberrations grew consisted of a corresponding mental personality. However, it was found also that mental reactions related to the schizophrenic, manic-depressive, etc., would develop on an organic basis, although in such cases other mental reactions, peculiarly organic, would be added to the clinical picture. The natural inference is that perhaps undiscovered organic causes may precipitate the reactions in the apparently endogenous cases, and yet be of such a different kind and location as to permit the omission of what we are accustomed to regard as the organic reactions. If this should ultimately prove true, it will be no reflection on the great work that has been and is being done in psychoanalysis, without which our present knowledge of mental operations would be less adequate than it is, and in particular we would know comparatively nothing of that great subsoil underlying the conscious and preconscious and referred to as the unconscious; nor would we possess an important therapeutic measure for obtaining curative effects in many cases and palliative in others of more malignant nature.

Kretschmer found that, associated with the special types of personality as described by Hoch and others, there was a preponderance of certain physical types. Thus we have an apparent tendency for types of psychogenic mental disturbances to be found in connection with certain types of both mental and physical constitu-

tion. A hasty conclusion would be that the latter definitely determine the former, but in the absence of authority to make such a deduction, one may with reason state that it is evident that such physical and mental constitutions have a special tendency to be affected with the type of psychosis with which we find them so often associated.

Added to this suggestion of a special physical basis, are some physical symptoms and signs found in many schizophrenics, such as lowered metabolism, vasomotor disturbances and pupillary changes—all possibly attributable to dysfunction of the vegetative nervous system working directly or through its influence on the endocrine system—changes in the endocrine glands, demonstrated post-mortem, and indications, from comparisons of the blood in the jugular vein with that returning from an extremity, of a reduced use of oxygen by the brain, this suggesting chemophysiological impairment of that organ. In this last connection, it is of interest to note that the inhalation of an atmosphere with greatly increased amounts of oxygen and carbon dioxide will, after brief other effects, temporarily suspend certain stuporous states and bring about the resumption of a transient and approximately normal behavior, and that experimental therapeutic attempts are under way by the use of a continuous administration of a modified atmosphere of the same character. The administration of sodium amytal will, after producing narcosis, cause a similar suspension and substitution. Contrariwise, it is of interest to note that in bulbocapnine we have a drug, the administration of which will produce in healthy mammals behavior which seems identical with these stupors; hence the inference that in psychotic patients such states may be due to some endogenous intoxication.

A hereditary predisposition in the etiology of these psychoses has been evident and formerly was regarded as rather direct and specific in its transmission. With greater exactness in diagnosis and better statistical studies, it is now found that there is a neuropathic incidence in the antecedents of the psychotic which is definitely greater than in the antecedents of the normal, but that the same type of mental disturbance is far from being universal in the ancestral psychotic data and that, instead of the same type being

transmitted, other mental abnormalities are also found. The tendency, however, is toward transmission from similar rather than from dissimilar psychoneuropathic heredity.

Attempts have been made to apply the Mendelian formula of inheritance to the incidence of these psychoses and the problem is not settled. In dementia præcox, for example, the irregular manner of appearance may depend upon two or more formative factors which may be recessive or dominant, the disease not appearing unless the necessary factors operate together, and the occasional association of dementia præcox and manic-depressive psychosis in inheritance may be due to one factor common to both.

It is still an unsettled question as to whether these disorders are fixed by inheritance through the germ plasm or are induced by the environment or the life difficulties and mental conflicts—in other words, acquired after impregnation of the ovum. If we could find individuals of exactly the same heredity, we could formulate a rule that in such cases the development of a psychosis in one and not in another would be evidence that the disorder was due to causes occurring after the beginning of the embryo, and, barring injury at birth, probably after that event. Likewise, should such equal partners in inheritance fail to show, even under diverse environmental conditions, variations in psychotic tendencies or in freedom from them, the evidence would point to the conclusion that the tendencies or the diseases were fixed by the germ plasm; in fact, the invariable presence or absence of the disease in the members of such sets of partners would strongly point to heredity as the determining factor of the disease.

Evidence points to our having such sets of equal inheritance in identical twins. The study of this kind of twins has helped to elucidate other problems relating to the question of heredity and environment.

Sir Francis Galton in 1883 in his pioneer work stated "Twins have a special claim upon our attention; it is that their history affords us a means of distinguishing between the effects of tendencies received at birth and those that were imposed by the special circumstances of their after lives."

In this country, Benjamin Rush in 1812, in his book on mental

diseases, cited a case of what was evidently manic-depressive insanity in two Revolutionary soldiers, identical twins, who were affected with "hereditary madness."

Since then, a number of instances of mental disease in twins have been reported, but usually the reports have failed either to state that the twins were identical or to offer proof that due observation had been made to establish their similarity. For example, the only report from the New York State hospitals was one by Smith, 1912¹, on several cases of concurrent insanity in twins, but there was no distinction made between fraternal and identical pairs. The psychoses appeared to be of the same type in what may have been two sets of identical twins and of the same type in a pair of unlike sex and therefore not identical. In his other cases there was available for study only one individual of each pair. A survey of the literature on psychoses in twins reveals a disappointing absence of a determination of identity or fraternity. It also fails to show, with only four exceptions, to be mentioned later, a report of a functional psychosis in only one in a pair of identical twins. More recently the literature shows a tendency to settle the question of identity, thus making the observations of value in this study.

Unfortunately, attention is more strongly attracted by instances of concurrent disease in any kind of twins, whereas the occurrence of a mental disorder in a patient ordinarily has not prompted inquiry as to whether he is a twin and particularly as to whether, in case of twins, the other individual is identical and affected at any time with a psychosis.

For purposes of this study, twins may be divided into two classes—monozygotic, uniovular, monochorionic, homologous, similar or identical, and dizygotic, binovular, dichorionic, heterologous, dissimilar or fraternal. The first are always like sexed while the second may be of the same or different sex; the latter, while showing a somewhat greater tendency to resemble one another than children of different births from the same parents, are often as unlike as these and in no case approximate a condition to justify the term "identical."

Homologous twins are strikingly alike in appearance and manner and this close resemblance is only slightly modified by environ-

ment and even less so by advancing age. Postmortem, the internal structures, including the brain, have a similar approximation. The criteria of identity are as follows: Same sex; close similarity of features, physical measurements, body build, hair color, texture and distribution, iris coloring and markings, skin color, texture and pigmentation, shape and size of ears, shape and irregularities of teeth; close resemblance or reversal of symmetry of finger tip patterns. The physical measurements may be modified in one twin by acquired disease or by malnutrition.

It is estimated by Dr. Joseph B. DeLee in his "Principles and Practice of Obstetrics," that twins occur in 1 out of 87 births and that uniovular twins occur in 15.5 per cent of twin births. It is probable that the rates vary considerably among different races and at different times.

Some have held that twins are the result of the impregnation of the ovum by two spermatozoa, as observed in ova of fish, but there are reasons to believe that the doubling is due to cleavage after the reception of only one spermatozoon. For instance, the mere shaking of ova of the sea urchin in sea water lacking in calcium will separate the blastomeres, causing the development of two individuals. In the Texan armadillo identical quadruplets are the invariable rule, and it would seem unlikely that four spermatozoa are regular participants in impregnation. Newmann² draws attention to the mirror imaging in the armor of the armadillo sets, as against the small tendency to such reversal symmetry in human homologous pairs, drawing the conclusion that the former become separated at a later period than the latter and thus are not so complete in the reorganization of the symmetry relations and have more residuum of original common symmetry. In 9 out of 45 homologous human twins, Siemens³ found symmetry of right or left handedness.

Homologous twins are not exact duplicates but are as nearly so as the two sides of the body of an individual. In both cases the percentage of similarity is estimated at ninety.

In the mental endowment of homologous twins the similarity appears of the same degree. Reports in this matter show parallelism in school ratings, abilities, temperament and mental reactions.

That their nervous system is general has equal similarity in

structure and operation is evidenced by striking likeness in manner, posture, gait, voice and behavior reactions.

The percentages of variation in the time and in the phenomena of mutual mental and physical disease are about the same.

As to the retention of these similarities after separation in infancy and rearing under different environment, a number of observations have been recorded. The Journal of Heredity,⁴ a few years ago, undertook an investigation of this matter and published data, among which were articles by Popenoe and others which showed how little the different environments had affected the original endowments. An example of special interest was found in a pair of orphan twins, separation of which had occurred at the age of eight months, the rearing following in divergent parts of the United States.

The incidence of identical twins, reared in environments of altogether diverse kinds, or under extremes of intellectual and moral training, is relatively rare, and data on this subject would elucidate the question of the comparative influences of heredity and environment on the individual.

Data on organic nervous disease, not of exogenous character so far as known, were collected by Wilson and Wolfsohn,⁵ who claim that there have been few published cases. They mention epilepsy and Friedrich's ataxia and describe, as coming under their observation, cases of congenital nuclear ophthalmoplegia, cerebral diplegia and epilepsy. Regarding this last disorder, only one instance has occurred at Craig Colony for Epileptics in which any kind of twins were known each to be affected with the syndrome and in this case the twins were homologous, and an impression exists that no adequate study of data has been published. This disease may, so far as known, have more than one etiology, and freedom from symptoms in only one of an homologous pair would throw additional light on the problem, provided each of the two individuals was subjected to equal environmental influences, and the post-mortem brain findings did not show acquired pathology. Likewise, the problem of mental enfeeblement—many homologous pairs being known—is complicated by the fact that one member of the set may be impaired during birth delivery or afterward by injury or infec-

tion, both of which are recognized as factors in the production of mental defect, and yet are not always determined in the history of a case.

Mongolism has occurred in one of twins, which is consistent with its non-consecutive appearance, and this shows a probable absence of etiology in the uterine environment. However, Archard,⁶ in quoting Halbertsma,⁷ states that the literature includes only five cases of twin mongolism and that all of these were of like sex, this number of observations being insufficient to prove, but enough to suspect, uniovulation in all.

Identical twins show identity in anomalies of development when such are present. Twin monsters, unseparated, and Siamese twins, always of the same sex, are uniovular.

Other diseases in homologous twins, not known to be of exogenous character, have been recorded as occurring simultaneously or approximately, such as cataract, leukemia, hemophilia, goitre, myxedema, pyloric stenosis, diabetes, cardiorenal disease, etc.

Resuming the consideration of psychoses in identical twins, Franz⁸ reported dementia præcox beginning in a pair at 20 years of age. Parker⁹ investigated this case further and satisfied himself that they were identical. He reported a second instance, the one developing insidiously from 16 to 19 years of age, the other apparently suddenly at 19, both receiving hospitalization at the same time but in different institutions. After 33 years they were both in the same hospital and it was noted that not only were their appearances sufficiently similar for them to be mistaken for each other, but their mannerisms were strikingly alike. Parker, director of Harvard University Zoological Laboratories, has recently written, in response to inquiry, that no further cases of the kind under attention have been learned of by him, nor has he been able to get evidence of a case in which only one of homologous twins had dementia præcox. He concludes that dementia præcox is germinal in origin.

Siemens, in his survey of the pathology of twins, collected seventeen cases of dementia præcox among them, six of which were undoubtedly in homologous pairs, five were doubtful and six were fraternal. He failed to find the disease confined to only one of an

identical pair; and in three of the six identical pairs found the onset "simultaneous," in a fourth a year in separation, and in the remaining two doubtful as to the interval between onsets.

Newel¹⁰ reported a case of homologous twin sisters, one of which was partially paralyzed from infantile paralysis, and who, with the occurrence of the incapacity, developed a lack of self-confidence, seclusiveness, feelings of inferiority to and jealousy of her twin sister, particularly as the result of suffering comments of comparison unfavorable to herself. While she did not develop a psychosis, her temperament was modified to one of general suspiciousness and her intellect was inferior, perhaps due to the same unhappy comparisons, although the poliomyelitis, which occurred at the age of two, may have extended to the brain, as, in spite of the fact that she had walked a few months earlier than her sister, she fell behind her sister in learning to speak after the disease and while relearning to walk, and formulated sentences three years later than her twin. In this case there remains the doubtful element of brain damage at the time of paralytic infection.

Rosanoff¹¹ undertook a study of mental disorders in twins about two years ago and has collected 305 pairs, in one or both members of each of which some mental disorder is present, but is continuing the inquiry until the cases are at least doubled in number. He finds that the reported data are few and that there is a lack of inquiry into the other twin's condition when only one is under observation for disorder, thus causing a lessened possibility of learning of a healthy monozygotic partner of a psychotic twin. His data include the noting of the three classes of twins (see below) and of the incidence of not only schizophrenia and manic-depressive psychosis but also mental deficiency, epilepsy, drug addiction, mongolism and delinquency. He has published preliminary reports. He found that both of twins of monozygotic type were affected in 86 per cent, in like sexed dizygotic 56 per cent and in unlike sexed dizygotic 21 per cent.

At last report, he had collected 35 pairs of twins in one or both members of which there was dementia præcox. Eleven were identical, and in these there were nine mutually affected cases and two in which one member of the pair is recorded as normal. In manic-de-

pressive psychoses he has data on 18 cases, among which are 8 that are identical, in two of which one member of the pair is recorded as unaffected.

There were 34 cases of mental deficiency in identical twins and in two it was noted in only one of the individuals. In three identical twins in which epilepsy was found one case showed a normal member of the pair.

There was only one instance of mongolism and that was a double incidence in an identical set of twins.

His findings will increase in value when further extended. Thus far he has collected data on the west coast and now is extending the work to the east coast. As a result of this, there may be an opportunity afforded to secure full data of the occurrences, if any, of schizophrenia or manic-depressive insanity in only one member of a set of homologous twins.

The writer wishes to record here a case of homologous twins coming under his observation. Details not essential to the general purpose of this thesis are included in order to render an adequate description.

Mrs. Mary L. and Mrs. Annie S. are twins; both have dementia præcox and are patients in the same State hospital. They are 47 years of age. The writer is satisfied that they are identical, for reasons stated below. Mary's personality is well preserved and she is able to give an account of the lives and characteristics of herself and sister. Annie is in a catatonic, negativistic state and can give no information. In spite of the lack of facial expressiveness of the latter, the close similarity of features of the two is striking and, to the writer, convincing. It is worthy of note that several persons who had been in contact with these patients before the writer saw them, when asked whether they were probably identical, stated that they evidently were not, as they did not look alike. This error was no doubt due to lack of critical comparison and to a substitution of dissimilar impressions from observing dissimilar behavior, Mary presenting quite a normal reaction, while Annie lay in bed, emaciated and stuporous. This is an example of the futility of gathering data on a basis of hearsay and without adequate details to prove either identity or fraternity.

While Annie's emaciation from her long catatonic state has reduced her from 153 to 100 pounds, she and her sister were of practically the same weight through adolescence. Annie married at 16, had several children and increased in weight. When Mary first saw her, reduced in flesh and after a lapse of years, she at first denied it could be her sister. Not only are the features of each—nose, mouth, chin, ears, contour—identical in size and form, but the eye color and markings, eyebrow form, and hair line are the same. The shade of hair is now slightly different but in early life they were regarded as having the same color and shade of hair. The skin, in color and texture, is the same in each. Finger tip and foot sole prints correspond in design although the arrangement of pattern in one great toe varies considerably. While Mary states that Annie wore a slightly smaller shoe than she and that her shoulders were not quite so broad, measurements now correspond almost exactly. Upper limbs measure the same and in both the left arm is the shorter. Their friends not infrequently did not readily distinguish them, and on one occasion, shortly after Annie's marriage, she induced Mary to read in her chair, to fool Annie's husband, who, when he entered, saw her and heard her voice and yet thought she was his wife.

Both completed common school at the same time and did equally well. They differed some; Annie was more "full of life, fond of pranks," whereas Mary was "quieter and liked to sit and read." It is not definitely known whether this difference was more than slight. The description of identical twins often shows a slight difference in temperament. The sisters enjoyed sports, dancing and singing equally. Like most identical twins, they were so fond of each other as to cause remarks about it.

Annie bore seven children. Her husband and an adult daughter died when Annie was 34 and seven years later her only surviving child, a son who supported her, also died. Over both events she grieved, and about two years later, after nearly a year in a hospital for cystocele and rectocele and while living alone, she gradually became depressed, over-religious and thought people talked about

her, but she did not give adequate information as to the content. She was then 43 and was admitted to the State hospital, four years ago. Somewhat later she developed catatonic stupor with ideas of food poisoning, cancer, and later, identification with the deity. After a brief remission she again entered a stupor, which has become more marked and persistent.

Mary, married at 25, bore a child and a year later, when she was 34, her husband died, after which she "worked out" at intervals, living alone with her son. Three years ago she underwent a hysterectomy and a year later sustained a fracture of the femur, but recovered. Late in 1930 she had no work, and at the same time developed a depression and the notion that she was followed and talked about, that her character was criticized on the radio, that the priest assisted men to spy on her, that her brother intended to shoot her, and that the priest, having killed her sister by fellatio, now intended to kill her. Her personality and intellect are well preserved. Her psychosis is dementia præcox, paranoid type, and appeared about three years later than the same disease in her sister.

These sisters were the only children, in a family of 13, to have a nervous or mental disorder, but only one of the others has attained the age period at which these two sisters developed psychoses. The history of the antecedents and collaterals is negative, on an inadequate basis.

The citing of this case is not expected to add to our knowledge of etiology but calls attention to the amount of variation, about three years, in the time of onset and to the variation in the clinical phases of what is evidently the same disease, one presenting a catatonic stupor, the other a paranoid reaction. Both of these divergencies are consistent with not only the variations in mental disorders in homologous twins but also with the chronological and clinical variations of other disorders in such twins. These variations are no greater, probably, than in the similar physical features, which are never absolutely alike—no more, as previously stated, than are the two halves of the body perfect duplicates.

CONCLUSIONS

1. Identical twins are equal in inheritance.
2. The study of the incidence of mental disorders in identical twins may be an aid in the determination of causal factors, and in distinguishing hereditary from environmental factors.
3. Dementia præcox or manic-depressive psychosis rarely occurs in only one of a pair of identical twins.

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THE PRESENT AND THE FUTURE OUTLOOK IN THE TREATMENT OF AMENTIA*¹

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We were first led to an application of Freud's depth psychology to amentia in finding that there were various fragmentary psychotic syndromes in many aments—in addition to the grand neurosis of the amentia itself. Our total work in this field has led us to make an individual report of all the main grades of mental arrest and point out the psychology of each stage of arrest. Using our findings in mental arrest we have attempted to formulate a scientific basis of intelligence in general. We believe that this dynamic approach will open the way not only for a better understanding of amentia but that it will be of signal value in all pedagogy.

This article upon the training treatment of feeble-mindedness is based upon our psychoanalytic research in amentia which in its case detailment will soon be incorporated in book form. Our general contention is that while amentia is possibly dependent upon an inherent or constitutional weakness in the ego, the defective libidinal distribution is of the utmost practical importance. We hold that the primary narcissism is too rigidly attached to the ego in the severer forms of amentia (idiocy); and that only in the milder grades of feeble-mindedness, where some degree of secondary narcissism obtains, can one hope to advance the ament toward a more adult ego and a greater object-cathexis. By a psychoanalytic understanding of his individual problem, we may be able to throw much light upon the inter-dependence of the ego and the libidinal forces in the process of mental functioning.

It may be surprising to many that very little advance in our ability to ameliorate the various states of mental arrest has come about since Seguin's monumental work in 1846. Following the introduction of his system there was an immediate progress towards the intensive training of all persons suffering from mental arrest. During the past several decades variations and en-

* Assisted by the staff of the Psychoanalytic Sanatorium at Stamford, Conn.

1. Read before the medical and teaching staffs of Letchworth Village and the Randall's Island Schools for Mental Defectives, July and August, 1932.

largements of his main theory and its practice have been made; but behind it all there seems to have developed the false hope that by this means one might eventually restore normal intelligence. Seguin himself never lost sight of the fact that the main goal was simply the full development of the individual child within the limits of his state of mental arrest. Yet those who had unconsciously been led to expect more turned away from his system with an extreme of disillusionment when the results were less than miraculous. The reaction was again to a more or less complete reliance on custodial care and industrialization of the feeble-minded in special institutions or colonies.

There have been those, more fancifully inclined, who have held out to parents the hope that these difficult children "will grow out of it." As a consequence they have planned an uncertain, waiting course which could lead only to ultimate disappointment and embitterment. Obviously in this attitude there is an unwillingness to face things as they are, and it can result merely in a failure to do for the defective all that can be done. On the other hand, parents and relatives who through pride will not allow themselves to face the truth have sought confirmation of the wish that their defective offspring be restored to normality. They have frequently fallen prey to all sorts of quackery or to designing persons who may urge upon them the magic panacea of "cure."

Between the two extremes of doing nothing for the mentally retarded and of hoping for a cure there would seem to lie an extensive field for research and conscientious endeavor. Can we understand more of the nature of mental arrest? While still granting that the ultimate cause is probably an inherent defect, is it possible in amentia to see dynamic elements which are more closely connected with the phases of everyday functioning and adjustment? Our approach to the problem has been based on the uses to which libido and other impulsive energy can be put, in the process of intellectually grasping the outer world and adapting to it. Recent studies have led us to postulate that in acquiring knowledge, the individual forms an identification with the person from whom he is learning or with the "thing" whose subject-matter he is "taking in." The ingestion and absorption of these identifications within

the ego is seen as leading to a use of the content in mastering or adjusting to reality. Our theory has been that the capacity for forming identifications is first manifested in the child's earliest relationships with the mother. The nursing period contains an aggressive impulse to engulf the mother by way of the mouth, to make her more completely a part of the child's ego. Further development displaces this ingestive process, from the oral zone to the hands and into the uses of other sense-organs of perception. Grasp, then, is still supplied energy from the oral libido and from the modified destructive impulses, but the grasping is no longer simply an oral "taking in." At first, to learn of a thing was to put it in the mouth or to touch and hold it in the hand. The identifications were necessarily with tangible objects, and their qualities were concretely learned about. From mother, the child takes on characteristics, mannerisms, methods, etc., which are still more or less tangible. But soon his power for identification grows to include abstract substances and extends to all phases of the outer world. The capacity, we feel, develops from ingesting mother to mentally acquiring other people's knowledge or abilities; from physically "taking in" concrete subject-matter to mentally grasping abstract ideas.

The first barrier against the forming of identifications is the primary narcissism, for its influence is towards an aloofness and a magic self-sufficiency. When libido is displaced from this into the secondary narcissism, there is a greater impulse to seek contacts with the outer world, for the need is to win more love for the ego. Yet, while secondary narcissism fosters a greater striving towards getting things from the outer world, it may eventually block the absorption of this acquired knowledge. The erotic component must not continue to dominate and keep the effort merely one for libidinal reward. There must be a re-projection of libido into an objective use of the knowledge; and when this takes place, the subject-matter is more fully merged into the ego to become an indistinguishable part of its power to function in reality.

In short, it has been our belief that libido-development, the growth of the ego, and the disposition of destructive impulses play a much larger part in mental functioning than has hitherto been

supposed. These elements do not constitute the whole problem of mental arrest, but their dynamic aspects surely have much to do with the energies which are available for intellectual use. An insight into their mechanisms may help us to understand the ament in his everyday efforts to get along in the world. Can our research and tentative formulations suggest anything helpful for therapy?

First, we might remark that the hope that followed ductless gland therapy, which was of such signal value to certain types of secondary amentia, has not been sustained in primary cases where no such deficiency of gland function can be found. In both classes various drug medications are also found to be useless. In secondary cases known to have been due to hereditary and even early syphilitic involvement, specific treatment is again of little avail. Surgical efforts may also be said to have failed for general application. Indeed, all forms of medicinal therapy may be dismissed with the comment that its use and results do not measureably alter the degree of mental arrest; nor is it different in application than that found effective in all normal children.

We come then to the training treatment as such, and here we find the Seguin system forming the basis or providing the essential aim in all education of those suffering from mental arrest. In his own words, it "consists in the adaptation of the principles of physiology, through physiological means and instruments to the development of the dynamic, perceptive reflections and spontaneous functions of youth." By this system and those similar to it each function and faculty of the mind is given graded, developmental training by means of detailed drill and careful mental of physical calisthenics. Not only are the sensory mechanisms educated but also exercises are given to aid in controlling the body, to develop the manual grasp, and to advance the general coordination. Moreover, the faculty of attention, of association of impressions, of perception of form and color, etc., are trained and put to use in drills. Mental ability depends so fundamentally upon proper sensation as well as upon the special senses and their adequate functioning, one sees at once how necessary it is to use all means possible to place these functions at their highest potential service. We

need not detail here, however, the carefully elaborated "intellectualization" of the senses which is a large part of this system, for more precise descriptions are at hand in any library upon the subject. Our attention must center on what additional understanding a psychoanalytic point of view can give to the useful phases of such a system, and what hints it may give us as to the possible dangers in the training.

It can be seen that Seguin's system and its various modifications contain a high degree of concreteness in the detailed drills and training for the feeble-minded. Our own formulations indicate that this is necessary, inasmuch as the ament is restricted in the range of his ingestion and absorption of knowledge. He has progressed little in the step away from physical or tangible identifications, such as in the grasping and "knowing" of mother, towards more abstract relationships such as include the ingesting of ideas and general conceptions. Since his capacity for absorbing identifications remains at the earlier stages of development, his education can be of more permanent value if it is concrete. It seems obvious from a study of the idiot that if he is to give attention to any new supply of knowledge, there must be a physical formulation of it. Some, for instance, are able to make progress by play-instruction with blocks; one boy, particularly, was receptive to memorizing nursery rhymes when the teacher engaged with him in a rhythmic clapping of hands. At a higher level we find that many even of the low-grade feeble-minded can grasp such ideas as storekeeping and making change, if in play sessions they have been instructed with actual commodities and real money. We may recognize that concreteness as such is not to be the sole aim. It may represent the field in which the retarded individual will make the surest advance, but it may also serve as a means towards eventually grasping more abstract understandings of reality. We should agree, however, that it is only from the basis of concrete illustrations and experiences that the ament can make progress.

Just as the feeble-minded require concreteness in their training, so they are found to need variety in the objects placed before them. From our theoretical formulation we can understand why this is found to be true in general practice. Since the forming of an iden-

tification requires the projection of libido towards the object, the more diverse and variegated these are, the more likely they are to capture the child's interest. We say that he learns the same thing in many different ways; or, in other words, he makes a series of separate identifications, all tending towards the same knowledge; each strengthening the worth of the other. With the mentally retarded we might observe that an unusual attractiveness from the object is necessary to lure the libido away from the primary narcissism; and that a greatly extended *number* of partial identifications must substitute for their lack of ability to attain a deep grasp and full absorption of any one identification.

But this does not mean that the same process should not be repeated again and again. Indeed, the constant repetition of situations and ideas is a fundamental requirement in teaching backward children. The amount of libido detached from the primary narcissism is so slight and uncertain that each identification must be frequently renewed in order that its substance may be firmly impressed on to the ego. Otherwise it seems probable that the retarded individual would find little occasion to project towards an ingestion of the objects to be understood. The libido would be withdrawn within the primary narcissism before it became firmly attached to the identification. Apparently the need, then, is to keep the ego in continual contact with the same identification. Progress must be slow, and the ground must be covered many times over before real advance can be claimed.

The fact is amply demonstrated in the case of a feeble-minded boy now under treatment. He is frequently able to do problems in arithmetic at the time they are explained and demonstrated to him. For weeks he may do fairly well on that particular problem. But let there be a space of several days when that kind of example is not mentioned, and when he returns to it he is often hopelessly at sea. Psychoanalytic data indicate that his primary narcissism has been loosened to some extent, but that much of his libido goes into clinging relationships which are to answer the ego's need for protection. He cannot maintain a consistent objectivity nor does he make a wide range of new identifications; hence, there is difficulty in absorbing the identifications he does make. As long as the arith-

metic is present as something he must ingest in order to answer a need of the ego (for the teacher's approval), it is kept as an identified object. But once the immediate need is allowed to lag, the identification is seemingly lost. What is required, apparently, is the opportunity to repeat this same identification constantly for months; and it is found that, in such instances, the boy makes a more nearly complete absorption of the subject-matter.

Doubtless similar experiences are to be found in every case of amentia. It may be interesting, however, to add what is especially observed in retarded individuals under analysis. Whereas the average person lives through the experiences and associations connected with his emotional tendencies, to come eventually to an insight into his own character make-up, the feeble-minded are seen to repeat the same material over and over again, unable for great lengths of time to absorb a real self-understanding. Obviously the proof of a true insight, whether completely conscious or not, is when the given tendency ceases to be a conflict. The retarded patient frequently manifests an attitude of "lip service" to the psychoanalytic interpretations, but his failure really to accept them is shown in the continued repetition of the same behavior difficulties. It seems apparent that a longer period of re-experiencing is required, before an identification with the insight may be fully ingested and absorbed as an indistinguishable part of the ego. Many cases are found where only after months of analytic play-sessions allowing full dramatization of anti-social activities does a change take place. There may be a professed recognition of reality-principles but the trend of feeling keeps its original channel even more constantly than in the ordinary neurotic. Only very slowly is it indicated that at last an identification with some phases of the outer world has been absorbed within the ego, so that a part of the impulsive striving has become more socialized. We should say, then, that if it is at all possible to analyze the feeble-minded, they certainly need much more time than the average in which to carry out such a process of absorption.

In addition to concreteness, variety, and repetition, our understanding leads us to suggest a further element in the training of mentally retarded individuals. According to our formulation, the

ingestion of identifications implies a projection of destructive impulses into an oral mastering of objects in the outer world. Practically all of our cases have indicated some perversion of this aggressive force. Either it has failed to become sufficiently fused with erotic impulses, and has thus kept much of its pure destructiveness, or it has been taken over by the super-ego in a harshness leading to varied forms of masochism and timidity. It seems important therefore that an opportunity be given for the child to relive the early stages of the destructive impulses, by means of activities in a controlled environment, if not in an actual period of psychoanalysis. Many of the modern schools for training carry this out when they place at the child's disposal innumerable objects which may be destroyed at will and without censure. Our point of view would lend commendation to this procedure, especially when it is accompanied by a not-too-hasty encouragement of growing sympathy on the part of the child towards the object attacked.

The teacher's attitude, we feel, should long be one of passive support or emotional understanding for whatever trends of destructiveness are expressed. Only slowly and in careful harmony with the pupil's vague tendencies, should such feelings as "pity" and "compassion" be aroused. By thus allowing a greater freedom for the violent impulses, one may help to avoid a fear-inspired repression of them and may foster a developing fusion between love and aggressiveness such as is needed in the grasping of knowledge. Where this is not ordinarily successful, the longer and slower process of individual analysis would seem to be our only sound method of releasing energy from the deeper fixations and making it available for use in mental functioning.

What is of equal importance but is less generally carried out in educational systems is that the feeble-minded be granted opportunity to live through the incomplete oral stages of development. Possibly this is more difficult to encourage in the school environment, but at least we can strive to refrain from a too-active censorship and repression of it. According to our understanding, the mentally retarded are constitutionally needful of a longer dallying with the auto-erotic phases of the oral stage than is the average individual. Much harm can be done by an over-hasty restraint upon

such activities as thumb-sucking, placing objects in the mouth, etc. The experience of many investigators (including Anna Freud) is that the quick stamping out of such crude oral characteristics merely results in driving them into deeper grooves, blocking the development of the child in later stages. We should add that this seems true not only for the purely physical manifestations of the oral stage but also for the symbol formations which we associate with the oral character make-up. Attitudes of acquisitiveness and receptivity from the outer world, if too narrowly inhibited, may easily fail to develop to levels of intellectual nursing and ingestion. In being severely cramped, they may harden into the fixed characteristics of the social parasite ("the world owes me a living," etc.) if not leading to an actual neurosis.

Fundamentally, the aim of all treatments for amentia is to contribute something to the strengthening of the ego. No matter how this is brought about, there must necessarily result a diminished need for a rigid primary narcissism and a greater capacity for objectification and the absorbing of identifications. It may be recognized, however, that the ego stands in the position of a central government whose power depends upon the efficient coordination of all its parts. Basically it is a bodily ego, and we conceive of it as coming into existence as a unifying and directing agent for all the scattered demands of the various organic spheres. From this point of view, then, we can understand the value of training the coordinated and purposeful use of different parts of the body, such as practiced by Seguin and his followers. In fact, the whole program of an "intellectualization of the senses" would seem to owe its beneficial results to the increased capacity it thus gives the ego for getting along in reality.

From the psychoanalytic point of view, the ego can also be built up by encouraging a freedom of expression and emotional experiencing on the part of the individual. Under actual analysis, there may come an unrestrained bubbling out of all the innermost conceptions and impulses. In the usual school environment for the feeble-minded there should be a similar lack of restriction on the child's own thoughts and formulations. He may thus not only be spared the silencing which will later make for timidity and depend-

ence, but will also have the opportunity to test his attitudes in reality and discover for himself their relative worth. In short, the more the ego can be left free to try out its own impulses and make its own restrictions (in accordance with reality and the standards of society), the stronger will it be for all phases of contact and understanding grasp of the outer world.

Yet it is often objected that a complete freedom of expression may lead to all forms of asocial acts—which would only serve in the end to deepen the child's difficulties with society. In actual analysis, as Melanie Klein has found, the facing of reality and the gaining of sound insight necessarily would mean the establishing of a self-discipline which would attain, in more cooperative fashion, the same results that society attempts to impose. But in cases where this is impossible or, as in a training school, where analysis cannot be attempted, what is to be the result of granting freedom to the child's impulses? Here it seems as though some active part must be taken by the teacher, to secure recognition of the usual social standards of conduct. Our suggestion would be, however, that such disciplinary attitudes be taken not in a spirit of punishment but of friendly guidance and assistance to the child.

As most of our cases show, the mentally retarded are either severely handicapped by a domineering super-ego or are impelled into various forms of conduct disorder because of the conflict between the ego's weakness and the disciplines harshly imposed upon it. If the outer object which urges the restraint (teacher) can attract the individual's libido rather than his fear (repressed sadism), it can be seen that there will be more likelihood of an identification with the guiding principle and an absorption within the ego itself.

In the study of a particular case, reported in detail elsewhere, we came to just such a conclusion. The patient's weak ego seemed to alternate between over-destructive, nagging attitudes (sadism) towards the mother, and cringing attitudes (masochism) towards the father and his own super-ego. We felt that if he could come under the influence of some strong but kindly person (analyst, teacher, etc.), he might make an identification which would eventually add real strength to the ego. But here, as with others, the

emphasis must be placed on the kindness more than the strength; for without it we believe discipline would merely accentuate the harshness of the super-ego and increase the timid aloofness from reality.

In general teaching, it has long been known that the giving of libido is an essential factor. Perhaps it has not been formulated as such, but has been recognized in practice under such terms as "making the subject attractive," "arousing the pupil's interest," "establishing friendly relations between teacher and student," etc. In training the mentally retarded, this attitude on the part of the teacher is agreed to be even more tremendously important; but the reasons for it may be briefly stated here.

The feeble-minded as a class are more definitely fixated on the primary narcissism than the average individual. Even where some libido has been detached from this omnipotent aloofness, one sees an apparent reluctance in taking on new identifications. The reward to the secondary narcissism must be immediate and abundant, so that the step forward may have an appeal and an assurance of protection for the ego. One boy, an idiot, was at first incapable of caring for himself in any way, and was regarded as impossible of control or direction. He knew nothing at all about dressing himself and could not tell one garment from another. He was unable to employ words or to understand them, in those rare instances when his attention could be gained. Those who were with him, however, were devoted in their care and eager to supply happy moments of play with him. The boy formed a strong bond of affection for his teacher, and gradually became more and more willing to give some effort to win her love and approval. Eventually he learned many words and he can now express his wants rather clearly. He has some success in dressing himself, and on the whole will be a "good boy" for the sake of those whose fondness means so much to him. An ability to understand simple words and questions is shown in his activities, and he has become capable of running errands of a not-too-complicated nature. This progress, we feel sure, would not have been possible if there had been no auto-erotic, playful experiences combined with the educative processes; or if there had been no constant flow of loving encouragement from

his teacher. In all cases it is apparent that the instructor must to some extent substitute for the mother, who inspired the first attachment by answering the narcissistic and auto-erotic needs of the child. The teacher may now "stand in the shadow" of this original identification by pouring libido upon the infantile ego. Only in this way can the child be led to accept the variations from the mother-ideal which are necessarily present in the new object. Each teacher, then, must represent something similar to the previous identification while at the same time presenting differences.

Whereas the normal child is capable of accepting fairly wide variations from the original pattern, the retarded individual must necessarily progress to new identifications in small steps. Not only is this true of identifications with persons but equally so in identifications with "things." What is to be ingested must vary only slightly from what has already been taken in; there must be slow advance and constant review. But above all, love must be given by the teacher and won from the child in order to overcome the primary narcissism and induce a projection towards identifications in a wider field.

But at this point there comes the hardest problem of all, one which is often not fully appreciated and understood. Once the libidinal relationship with the teacher is secured, the pupil very frequently becomes closely attached. It would seem as though little could bar the way to progress; yet it is found that only slight advance is made. Even where the child does perform the tasks required of him, it is often clear that he has not made his knowledge an inherent part of himself that he may use outside the class room. We have studied one patient who uses his acquired knowledge, not for reality purposes but as "tricks" to exhibit for attention; another does his arithmetic merely to win the teacher's approval; and a third takes on adult attitudes, not naturally but for magic self-aggrandizement. In these instances, as in general, the retarded individual may make his identifications mainly for the reward of love; he frequently drinks in the libidinal values but fails to absorb the substance of what is being taught.

Here it is, then, that the teacher must go a step further. It is not enough to win the child's affection, so that libido passes freely

from teacher to pupil and back to teacher again. The child's projection of libido must be displaced from the person of the teacher and directed towards the work at hand. The thing to be done or the idea to be grasped becomes of the nature of a fetish, in so far as it substitutes for the loved teacher. Going beyond a mere performing for reward, the activity becomes something which in itself attracts libido and gives a narcissistic (and auto-erotic) return. The acquiring of new capacities and accomplishments then offers its own libidinal reward. But one further step is finally required: to separate the ingested substance (the "knowing how to do," etc.) from the excessive erotic element attached to it. The objective discharge of libido into the using of this knowledge in constructive activity must be developed. In this way the subject-matter, the accomplishment, etc., are fused into the ego as part of its capacity for dealing with reality. The identification has been absorbed; the material may at last be said to have been "learned."

It can be readily seen that inducing the pupil to project objectively into the work at hand (without over-abundant narcissistic and auto-erotic return) will offer the utmost difficulty. So much depends on the ego's being strong enough to do without its former libidinal safeguards, that the problem seems to be almost exclusively something to be worked out within the individual, rather than anything that can be given by the teacher. Probably the most that can be done under ordinary circumstances is, as we have mentioned before, to place no barriers in the way. The opportunity for a reasonably free experiencing of reality, under no severe restrictions of fear, may help many children to build up a sense of friendly confidence towards the outer world. The ego may attain a feeling of ability to cope with the environment, and thus may require less narcissistic protection. If, as is often the case with the mental defective, such ordinary measures are not enough, it would seem as though a period of individual analysis might offer some chance of relieving the ego of its deep fixations.

Psychoanalysis as a therapy would not claim to remove the fundamental causes of amentia. It would attempt, rather, to reduce the amount and depth of fixation so that the excessiveness of retardation may be avoided, even though the innate defect is not cur-

able. It would hope to enable the patient to use such levels of development as he can attain, for a socialized functioning in reality. Indeed, many critics may argue that our approach deals mainly with neurotic elements rather than with the amentia itself. We must grant a degree of fairness to the criticism and confess our inability to refute it. Yet we hold that the main consideration is the releasing of energy for projection into a grasping of reality and a satisfying adaptation to it. There may be cases where neurotic trends are not established but the general distribution of libido is such as to restrict the dynamic forces available for intellectual use. There will be many other instances, of course, where an actual neurosis or a conduct-disorder must be relieved first before mental development can proceed to its full potentialities.

In one case it was found that a fear-neurosis led to such a rigid system of narcissistic defense and compensation that the ego could not function freely in grasping and using knowledge. Another patient's conduct-disorder was seen to contribute greatly to the barriers against a full testing and understanding of reality. In neither case was the amentia caused by the neurosis, but the distribution of impulsive energy was such as to rob the ego of the dynamic forces necessary for whatever mental progress was inherently possible. In cases of secondary amentia, it seems clear that analysis might reduce the crippling effect of the disease, or, by freeing energy from an over-compensating protectiveness, delay the inevitable deterioration. Even where it is difficult to designate any definite relationship between the neurosis and the amentia, the possibility of any mental advance seems to depend greatly on how much the inhibiting neurotic factors can be stripped of their libido. In short, a degree of straightening out the psychic difficulties of the individual may at least serve to place more energy at the disposal of educative processes. Conversely, unless the inner conflicts of the individual are understood and taken into account there seemingly can be little true progress in mental training.

Apparently it is at this point that many of the usual methods of handling the feeble-minded meet with failure. The attempt is made to enforce with the child a moral and intellectual discipline which he is often incapable of meeting at the time. Since it is pressed

upon him from the outside, and without understanding of his deeper needs and patterns, it can only result in a more rigid in-binding of the fixations already established. A psychoanalytic approach, on the other hand, would attempt to foster within the individual a self-discipline such as he is ready to build and is willing to incorporate. Even in instances where this is impossible and where control is necessarily exacted from the outside, a real understanding of the child's make-up can insure a more enlightened guidance on the part of the teacher. Yet that this is not regularly followed out in usual practice is shown by the fact that in treating cases of amentia the first step must very often consist of undoing the work of previous educators. Otherwise the element of fear (often hidden from superficial view, yet deeply ingrained as a result of excessive disciplinary measures of the ordinary program) must inhibit the child's acceptance of reality. We need cite but two examples. In one feeble-minded boy the ego had remained too weak to sustain against the father a sadistic hate which might later have led to compromise in socialized attitudes of aggressiveness. Instead, he exhibited a strong tendency to turn the destructiveness against himself, and his masochistic trend was shown in moods of deep depression or in violent tantrums consisting mainly of physical self-injury. The enforcement of external control served merely to deepen his sado-masochistic hostility towards the outer world. In another case, a boy only slightly retarded, the emotional fixation at an oral-erotic stage had not been understood by those around him; and his irresponsible destructive tendencies had merely been condemned without insight. His reaction to the disciplines of parents and teachers had continued to be one of fear and inadequacy. In both of these cases, the usual directive or educational attitudes of the outer world had continued to raise further barriers against the possibility of grasping and absorbing parts of reality.

Even in the benevolent system of Seguin and those who have followed him, there would seem to be an element of compulsion. Although with the best of intentions and a most constructive purpose, the instructor appears to force upon the individual a program of development which the latter may often be unwilling freely to accept. It is our impression that here it is not out of love for the

teacher nor from inner needs, that the child takes on the new abilities; it is because the outer world offers him no choice. Seemingly, the danger under such circumstances is twofold. The pupil may be pushed into a series of identifications which allow him mechanically to act out the performances required, but in which the substance is not absorbed into the ego. Secondly, since the ego has not taken the initiative, it may be that a pattern of compulsive activity and timid dependence will later arise out of this training. In other words, progress may be attained at the *expense* of the ego rather than to its constant development; the toll may be a neurosis in later life.

Finally, we must recognize that the feeble-minded are very often handicapped by elements within the teacher's own personality. The work of training aments is so demanding that it necessarily requires a tremendous projection of libido into their care. Yet no one may deny that those who are entrusted with this process gain an enormous libidinal advantage from their work, to a degree which perhaps no other work among children affords. This is to be expected, for are we not here dealing with a condition which in more or less fixed form represents a continuance of infancy? How may we honestly evade the fact that it silently appeals to our enduring desire to play a benevolent, super-parental role towards children who may never grow up? Very frequently it happens that the teacher's own libidinal needs unconsciously exert a cramping effect upon the full, independent growth of these "permanent children." Much as a mother's emotional needs often tend to "spoil" a child, so the teacher's love-life may be too completely carried on within the teaching process. Hidden by rationalizations, "a wise protective care" may imperceptibly degenerate into something which fosters a constant, dependent clinging on the part of the pupil. That which the teacher has need of may thus be satisfied; but that which would allow the child to develop has been sacrificed.

The failure of the teacher to be aware of her own emotional tendencies is all too patent in many of the usual training systems. (Of course, this is not confined to women teachers alone.) Not only is the attitude towards the mentally retarded frequently too protective, too soft; but also there is very often an indulgence in the oppo-

site extreme. Disciplinary methods become too harsh and cold, too "hard"—possibly because the teacher's own super-ego has remained over-severe. Through identification she then restrains the child with the same stern repressiveness which she directs against her own ego. In other words, her own conflicts are unconsciously projected into the relationship with the pupil.

In many instances the teacher is seen to impose her own standard of values upon the child. Her pattern may be serviceable and sound, for her; yet, for another, it may be a distinct disadvantage. Moreover, if the instructor's emotional conflicts are mainly unsolved, there is danger that in the mutual identification with the child the latter may take over neurotic attitudes towards life. So-called normal children can more successfully battle against these unhealthier trends in the teacher's social and moral training; but the defective is less capable of keeping his own balance. A similar situation is seen in the usual analytic relationship, when the analyst's neurosis may exert an inhibiting effect upon the patient; for here, too, is a personal attachment which carries emotional values for both participants.

The problem is met in the analytic situation by requiring that the analyst himself shall have first submitted to a personal analysis. This, from our point of view, would be the ideal to be sought for in all teachers, especially those responsible for the training of aments. Obviously, it is of prime importance that the teacher not only understand the child but that she should also understand herself. Yet we must recognize that circumstances at present make it possible for but few teachers to be analyzed. At least we may suggest, however, that those selected for the care of the mentally retarded be ones who by nature are endowed with a fairly normal libidinal life. Since this too is probably an impossible condition, perhaps all that can be hoped for at this time is a conscious striving towards the attitudes recognized as ideal. The teacher may lend encouragement to objectivity and real, independent growth on the part of her little charge. She may strive to be impartial and impersonal, in the sense that her own problems shall not too completely envelop the child. Yet she must be aware that this tendency of hers will always be present, since it is this very trend of emotion

that impels her towards the task in the first place. Finally, although she becomes in all respects a kind and sympathetic parent, she must be able to adjust to the inevitable weaning. Possibly the mentally retarded are fated always to retain some degree of their infantile patterns. The teacher may keep open the way towards progress, however, if she becomes an understanding guide rather than a permanent parent to permanent children.

II

In one sense our application of the depth psychology of Freud has merely stated what was already known in another way. We have tried to give new support to this knowledge, however, by placing it on a more dynamic basis. Moreover, many of the mistakes in present-day training methods have often been vaguely sensed by teachers themselves; we have simply attempted to offer a reasonable explanation from the psychology of human beings. But, most of all, our research has aimed at evolving a tentative theory for amentia which, while encompassing the observations of the past, may open the way for more enlightened investigation in the future. It is for this reason that we have not hesitated to speculate freely where final, definite evidence is not available. It can be our purpose to keep the subject open, to remain receptive to new ideas and free to test them in our actual experience. Only in this manner may we avoid the unscientific rigidity of a closed mind, only from such a point of view may we hope to resume the progress in understanding amentia which Seguin so definitely advanced in his day.

A theory for the energy required in mental functioning seems necessary if the future is to see a deeper understanding of the ament's everyday problems. It is our belief that the development of inter-related trends of libidinal and destructive impulses, together with the ego's capacity to use them, supplies such a dynamic formulation. Briefly, our conception has been that the reduction of primary narcissism allows the libido to flow more freely into the formation of secondary narcissism, a trend which fosters an initial effort towards the outer world for the sake of reward. Further, a fusion between oral-erotic and destructive impulses gives this relationship a quality of ingesting the object, of forming an

identification with it, and of merging certain aspects of it within the ego. The individual thus gains a libidinal return and brings to himself, both from persons and "things," an added way of knowing and coping with reality. Finally, we have held that the reproduction of libido into objective uses serves to separate the acquired knowledge from its erotic component, and leads to an absorption of the substance into increased ego-power. This capacity for engulfing and digesting identifications is regarded as the foundation for mentally grasping the outer world, and its development is seen to depend greatly on the important trends in instinctual as well as ego development.

Postulating this and knowing the main trends of emotional growth, psychoanalysis may offer its help in several ways. Directly, it may be used as a form of individual therapy for the purpose of restoring flexibility and progress in emotional trends. It may thus release energy for a broader use in mental functioning. More generally, psychoanalytic principles may be applied towards a better understanding of the ament's difficulties and a more effective or purposeful training treatment. We have called attention to the reasons why such qualities as concreteness, variety, and repetition are found necessary in educating retarded individuals. We have stressed the importance of unconscious and libidinal trends in the psychological relationship between teacher and pupil. In doing so, we feel that a start has been made in the direction of wiser care for the feeble-minded. Future research may arrive at a wider elaboration of the formulations and suggestions outlined here.

A third field of advance is made plausible from the possibility of understanding better the total personality of the ament. For practical purposes it would be valuable if one could judge which channels of occupation and what environmental conditions will be best suited to the abilities and needs of a given ament. In the past these estimates have been based largely on the intuitive judgment of experienced workers, or have been evolved through the slow, uncertain process of trial and error. We have tried elsewhere, in case-studies too detailed for mention here, to foresee what future circumstances will be most favorable for the individual's general progress and serviceability. As much as possible these prognostic

formulations were based on psychoanalytic knowledge gained from treatment and observation of the given patient. At present these efforts are still not far removed from a dependence on "trying and seeing." Yet we wonder if in the future something more cannot be done in this direction, to make psychiatric advice more definite, more exactly a science than an art.

Psychometric tests can be of great service in determining the paths along which a feeble-minded person has his greatest natural ability. If the testing aims to discover not merely age-rating but the definite fields in which the individual is capable, there will be the possibility of restoring the ament to a useful position in society. Perhaps he can never establish himself on an equal plane with his normal fellows, but under favorable circumstances he may be able to attain some degree of real worth and constructive service. What is needed, apparently, is a formulation of the capacities necessary for specific kinds of occupations. The performance tests may then attempt to reveal the direction of the individual's greatest efficiency. In other words, psychometric testing might hope to determine the trends of ego-capacity and the kinds of identifications for which a person has the surest inclination.

For this we might gain further insight by understanding in new ways the individual's hereditary endowment. At present, in detailing a specific case-study it is very often of little value to cite the family history. In a large number of instances the factor of family-stock is found to be negative, and no data are on hand to suggest what inherent possibilities for development lie open to the patient. As long as the records of inheritance mention only outspoken diseases or clearly formed mental disorders, we feel that their usefulness in understanding the ament is very limited. If one could know, however, that certain ego-patterns or trends were manifested in the family, that specific kinds of identifications in the outer world were more easily formed than others, the data would clearly be important for guiding the individual's training. It may be that the future will see a deeper knowledge of the definite capacities which the ego inherits, and these facts may supplement the psychometric data in amplifying our understanding of how best to help the ament.

When modified psychometric tests and more purposeful studies of inheritance are supported by an application of our knowledge of the dynamic phases in mental functioning, one may eventually be able to judge accurately the most advantageous field of advance in a given case. It may be possible psychoanalytically to prescribe the occupational interests and circumstances for which the individual's instinctual trends and traits of personality are most ready. That is, the vagueness with which we now give our estimates may be supplanted by a greater certainty and a more directly helpful guidance. The libidinal and other impulsive trends may at some time be better known in their relationship to performance in certain occupations. Psychoanalysis has already formulated the fixations which lead to phases of personality such as "the oral character," "the anal type," etc. May it not further elaborate an understanding of the factors in emotional development and character-formation which serve to prepare or disqualify an individual for certain aspects of practical performance? Moreover, there may come also a clearer perception of the ways in which the environment may respond to the ament's libidinal needs and thus insure him a greater degree of happiness in adapting to social conditions. By thus encompassing the whole range of the individual's endowment and development, our knowledge may in the future make possible a higher level of aid to the feeble-minded.

The present study cannot hope to have established new truths nor to have determined new methods of approach. That will remain for further experience to evolve and test. Our goal has been to suggest interpretations of the observed facts in amentia, and to submit possibilities for future advance in helping the ament. If in doing this we have stimulated a deeper consideration of the retarded individual's plight; if we have focussed attention on the need for further knowledge of the ego-structure and its dynamic components; and if we have also aroused thought concerning all phases of normal or abnormal education and functioning—then we have more than served our purpose.

Our research still leaves us with many questions. Often, for instance, one is tempted to say that all people have fixations, that the feeble-minded merely have them to a greater degree; or that

everyone has defective capacities, but the ament is handicapped to a wider and deeper extent. Undoubtedly this quantitative factor is of the utmost importance, but is it the only differentiation between normal mentality and feeble-mindedness? Is there not a qualitative element, as well? Again, when we indicate an "oral fixation," what is it which decides that this shall in one case contribute to mental arrest, in another to a psychosis, and in a third simply to the establishment of an "oral personality"? Obviously other factors enter to play a determinative part, but is there something also in the *nature* of the fixation itself? Similarly, while the average individual makes wider and deeper identifications than the retarded person, is there also a difference in kind? Is this qualitative difference in identifications to be attributed to certain needs and tendencies of the ego?

We are loth to end our consideration of mental arrest at this point, but following the wisdom of Freud, " * * * We know already that, owing to the interdependence of the complicated problems of the mind, we are forced to break off every investigation at some point until such time as the results of another attempt elsewhere can come to its aid."

TUMORS OF THE PITUITARY GLAND AND ITS NEIGHBORING STRUCTURES*

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No discussion of the tumors of the pituitary gland and its neighboring structures can be entirely comprehensible without at least a preliminary sketch of the physiology of this extraordinarily complex organ. Forty-five years ago, when Pierre Marie¹ first described the disease, acromegaly, practically nothing was known of the function of the hypophysis. Marie himself was many years in becoming convinced as to whether or not the disease, which he so ably described clinically, had anything to do with the pituitary gland—and after that, many more years in deciding whether or not the glandular disturbance was one of overactivity, underactivity, or merely a bizarre pathological activity (so-called dysfunction).

Slowly, anatomical evidence began to pile up suggesting, in the first place, that some abnormality of the pituitary was always present in acromegaly and that this abnormality was usually in the form of a tumor.

The first logical deduction, therefore, was that the presence of a tumor must mean the destruction or displacement of the normal gland, and that acromegaly must, therefore, be an expression of depressed function of the pituitary. Indeed, it was this thought that led Victor Horsely to attempt a removal of the pituitary in dogs in order to reproduce the disease experimentally. Meanwhile, interest in the pituitary region grew and it soon was shown that certain cases of pituitary tumor exist—sometimes a very large tumor—in the absence of acromegaly; in fact, in patients showing symptoms antithetical to those of acromegaly. Further studies revealed that the pituitary tumor associated with acromegaly is an adenoma. By 1900, Benda² was able to prove that the adenomatous cells in tumors of acromegalics contained acidophilic granules resembling in appearance and staining reactions, those found in certain cells of the normal gland. These cells, while present in the adult, are especially abundant during the most active growth period in childhood. Adenomas occurring in non-acromegalic pa-

* Presented before the Bronx County Medical Society, December 16, 1931.

tients usually consist of agranular cells. Still a third type of cell in the normal anterior lobe of the hypophysis—namely, the basophilic cells—seldom gives origin to tumors.

The conclusion was inevitable, therefore, that just as the thyroid tumor in Graves' disease gives rise to symptoms of overactivity of the thyroid, so the adenoma of the pituitary in Marie's disease creates symptoms of overactivity of the latter gland. It was thus assumed that the overgrowth of the features and extremities of the entire skeleton and in fact, of the viscera as well, was a sign of this overactivity. The function of the pituitary in the regulation of growth was thus deduced.

The next link in the chain was produced by the results of experiments of Cushing and his co-workers, and of Aschmer in 1909 and 1910. Following removal of the anterior lobe of the hypophysis in dogs, the animals showed adiposity and gonadal as well as thyroidal dystrophy, and if young animals were chosen, an arrest in skeletal growth as well. Here, then, was a syndrome, experimentally produced by depriving the animal of its hypophysis, the antithesis of acromegaly, and was, therefore, named hypopituitarism.

Successful replacement therapy with pituitary glands or extracts in hypopituitary animals or patients was delayed, however, until Professor P. E. Smith accomplished it first in hypophysectomized tadpoles in 1923, and later in hypophysectomized rats. A few years earlier, Evans and his co-workers (1921) had been able to produce gigantism, a condition closely related to acromegaly, while working with normal rats by intraperitoneal injections of extracts of the anterior pituitary gland of cattle. While the final triumph of experimental pathology in this field was attained in Cushing's laboratory where the intraperitoneal injection of extracts, similar to those of Evans, resulted in the reproduction of acromegaly itself in normal dogs.³

So much, in brief, for the rôle of the pituitary as a growth-promoting influence. It had been recognized from the beginning that, associated with abnormalities of growth in diseases of the pituitary, are disturbances of gonadal function; the exact evaluation of which even today is not quite clear. While disturbances of the growth controlling mechanism of the pituitary gland may find ex-

pression in as widely contrasted conditions as gigantism and dwarfism, both clinical types may show an apparently similar gonadal dystrophy. Since it has been shown that the excessive growth in gigantism and acromegaly is associated with adenomata consisting of cells containing acidophilic granules, it is not unreasonable to assume that the gonadal stimulating factor may be a function of the cells bearing basophilic granules. What is more, Teel⁴ has recently reported a very rare case of a small pituitary basophilic adenoma in a patient who showed enlargement of the ovaries with a history of menses beginning at the age of nine, and consisting of excessive hemorrhagic discharges. All this still leaves unexplained the clinical facts that cases of pituitary adenoma consisting of cells with acidophilic granules and associated with gigantism or acromegaly, as well as those consisting of agranular cells and associated with skeletal infantilism, both show genital dystrophy. Some light has recently been thrown on this seeming anomaly by Henderson,⁵ a young Scotchman working in Cushing's clinic, who has been able to demonstrate, after studying 367 cases of pituitary adenoma, that the onset of genital dystrophy in cases of pituitary tumor with either hyper- or hypopituitarism coincides with the enlargement of the sella turcica. As a result, he advanced the view that "sexual dysfunction may be assumed to be due solely to the compression of the basophilic cells by the space-occupying lesion, whether the acidophilic cells remain active (as in acromegaly), or are also compressed (as in adiposo-genital dystrophy)." Favorable to this mechanical view of the process is the fact that the normal menstrual cycle may be resumed and pregnancy occur after successful operations with radical extirpation of the adenoma, in either type of case.

The bricks of this apparently harmonious structure concerning pituitary function were not permitted to rise, however, without dispute. Already in 1904, when the conception of the hormonal activity of the pituitary body was just beginning to assume considerable importance, Erdheim suggested that the adiposity, polyuria, and sexual dystrophy of Fröhlich's syndrome (believed to be due to hypopituitarism) really represented a lesion of the hypothalamic region of the brain, and was, therefore, a neurogenic symptom complex.

In 1920, Camus and Roussy⁶ and in the next year, Bailey and Bremer,⁷ brought experimental evidence to substantiate this view. They showed that injury to the hypothalamic region without disturbing the pituitary gland itself, resulted in the dog in adiposity, polyuria, and sexual dystrophy. Here again, Professor Smith⁸ stepped in with his clear cut experiments on the rat, and allocated the functions that are primarily pituitary and those that are primarily hypothalamic. The rat, unlike the dog, has a diaphragm separating the sella turcica from the cranial cavity except for a small opening for the infundibulum. By developing a transphenoidal approach to the rat's gland, he was able to remove it completely or in part without injury to the hypothalamus, and by an intracranial approach to the latter, was able to injure the hypothalamus without disturbing the pituitary.

The results of the experiments consisted of two clear-cut syndromes. Those rats from which the pituitary was ablated showed:

1. Complete cessation of growth in young animals, and progressive loss of weight in adults.
2. Persistence of sexual infantilism in the young and atrophy of the genital system in adults in both sexes; and
3. A profound atrophy of thyroid, parathyroids and adrenal cortex.

The rats with intact pituitary but with injury to the adjacent brain showed extreme adiposity, polyuria, and some genital atrophy. There was no atrophy of thyroid or adrenals, practically no dwarfing, and sexual cycles were frequently present. Moreover, replacement therapy which was effective in restoring a normal state in the hypophysectomized animals, failed to affect the latter at all. We have, at last then, as a result of the work of this brilliant investigator, a clear conception of the separate functions of the pituitary gland and its neighboring brain tissue. Clinically, the confusion apparently must lie in the close proximity of the structures so that a lesion, especially a tumor, affecting the one probably disturbs the function of the other. In addition, this very proximity suggests a certain functional interrelationship. We are aware that the pituitary body is joined closely to the nervous sys-

tem by definite nerve pathways and a lesion in the one may readily interrupt the activity of the other.

With the above as a background and in consideration of the other important structures in the neighborhood of the pituitary gland such as the optic chiasm, the circle of Willis, and the carotid arteries, the diagnosis of a tumor in the region of the pituitary gland in a general way should not be very difficult. It will be evident, nevertheless, that the diagnosis of tumors in this region with their specific character, point of origin, size, and direction of growth will often present fascinating but intricate problems. And from the point of view of the neurosurgeon such specific diagnoses are essential to guide him first in his decision to operate at all, then in the operative approach, and in the prognosis as to the chances of curing the patient, for upon the latter, depends the surgeon's judgment as to how much risk to take in attacking the lesion.

In the order of their frequency, the common lesions of this region are:

- Pituitary adenomas of both types
- Craniopharyngeal pouch cysts
- Suprasellar meningiomas
- Gliomas of the optic chiasm
- Chronic arachnoiditis
- Aneurysms of the circle of Willis

and a number of much rarer conditions such as

- Chordomas
- Angiomatous malformations
- Cholesteatomas, etc.

which need not concern us here.

DIAGNOSIS

Pituitary adenomas: Tumors arising from the pituitary gland as such are almost always adenomatous growths originating in the glandular substance of the anterior lobe. The symptoms are double in character and begin to manifest themselves in patients after puberty. The first variety of symptoms which is common to all types of adenomas is that of local pressure upon the optic chiasm—resulting in primary optic atrophy and bitemporal visual field de-

fects. Occasionally, one of these adenomas extends beyond the bounds of the enlarged sella turcica and invades the brain. Here it may amass sufficient bulk to bring about symptoms of increased intracranial pressure. Headache is a common symptom, however, even when no intracranial extension has taken place. This is believed to be due to tension applied to the dural diaphragm covering the sella turcica as well as the dural capsule of the gland as a result of the expanding intrasellar adenoma. X-rays of the sella usually show a widening of the intrasellar space with erosion of the clinoids and depression of the sellar floor.

The second variety of symptoms is dependent upon the disturbance of the normal function of the pituitary gland. The striking picture presented by patients with acromegaly is too well known to require any description.

A clinical picture, the direct contrast to acromegaly or gigantism—the typical adiposo-genital dystrophic individual—may, nevertheless, be almost as classical a sign-post pointing to a tumor of the pituitary gland as the former type. The difference is in the type of tumor. Dott and Bailey⁹ have called attention to an intermediary clinical appearance:

Patients that are above average height, with rather large, but well-formed extremities, inclined to be fat and flabby, with pasty complexion and sparse hair. Bailey and Cushing¹⁰ have shown that the adenomas in these cases are also intermediary between the type seen in acromegaly and those in pure hypopituitary cases. Dr. Cushing has frequently made the analogy between these various clinical pictures all associated with pituitary adenomas, and the differences in the degree of thyroid activity all associated with tumors of the thyroid gland.

Aside from the striking difference in physical appearance between the hyperpituitary and hypopituitary patients suffering from hypophyseal adenoma, there also exists marked variations in their metabolic processes which have been stressed by recent authors. Thus, the basal metabolic rate in acromegalics has been shown to be usually increased, by Boothby and Sandiford,¹¹ Cushing and Davidoff,¹² and others. The basal rate in hypopituitary cases, on the other hand, is usually depressed. The last named

authors have been able to show, moreover, that following operative removal of part of the hyperactive gland of acromegaly, the basal rate of metabolism takes a decided drop. These authors also have published some interesting data on the improvement in the lowered sugar tolerance of acromegalics after operation. Indeed, Ellis¹³ has reported a case of severe diabetes in an acromegalic which cleared up spontaneously after operative removal of the tumor. As might be expected, hypopituitary cases have a lowered basal rate of metabolism and a normal or increased tolerance for carbohydrates which are usually not affected by operation since this does not serve to restore the pituitary functions, but simply to remove the enlarged, inactive gland.

Craniopharyngeal pouch cysts: Congenital cystic tumors of the suprasellar region, especially the so-called adamantinomas, are so situated that they may produce pressure upon the hypothalamic region as well as the pituitary body. They usually, although not invariably, begin to manifest their symptoms early in life. The symptoms are again of two kinds, those related to pressure upon the chiasm which results in primary optic atrophy and bitemporal hemianopia; and those referable to the pressure effects upon the hypothalamus and hypophysis. The latter are usually in the form of sexual and skeletal infantilism, adiposity, high sugar tolerance, low basal metabolic rate, and sometimes diabetes insipidus. Quite occasionally the growth rises sufficiently high to invaginate the floor of the third ventricle enough to close off the foramina of Monro. When this happens symptoms of increased intracranial pressure occur, including a papilledema superimposed perhaps upon a former primary optic atrophy.

Since these cystic growths usually rest above the sella turcica, the latter frequently escapes enlargement or distortion as evidenced by roentgenography. In fully 80 per cent of the cases, moreover, according to Cushing, a shadow cast by the calcium deposit within the cyst wall is demonstrable, and is of considerable value in the diagnosis.

Suprasellar meningiomas: This is a lesion which, because of its usual failure to change the outline of the normal sella turcica, must be differentiated from the preceding group. It occurs generally

in middle-aged or older people, and arises from the tuberculum sellae so that, while it commonly gives the classical signs of optic atrophy and bitemporal hemianopsia, it is too far forward to involve to any degree either the pituitary gland or the tuber cinereum so that disturbances of glandular or vegetative functions are practically always absent. In addition, it seldom casts a calcium shadow on the X-ray film. Thus, an otherwise normal middle-aged individual with a normal-looking X-ray picture of the skull and with primary optic atrophy plus bitemporal hemianopsia is more than likely to be harboring one of these meningeal tumors.

Glioma of the optic chiasm: While the optic nerves and chiasm may often suffer from pressure of tumors originating elsewhere, they may also be the seat of primary tumors, especially gliomas. Reports of such cases usually appear in ophthalmological literature. But these are practically always cases in which the tumor arises in the ocular portion of the nerve and extends backwards. In 1923, Martin and Cushing¹⁴ reported 7 cases originating in the chiasm or the post-ocular portion of the optic nerves. These cases are sometimes difficult to diagnose at all, and those in which the general site of the growth is suspected are usually confused with cases of congenital cystic tumors of the suprasellar region. Four of Martin and Cushing's cases were in children under ten years of age. In practically all, loss of vision was rapid and progressive, blindness in one eye was common on admission; one patient was totally blind. The visual fields in the three adults showed temporal defects in the good eye, but none showed the clean-cut vertical bisection of the field so characteristic of pituitary tumor. Roentgenograms which, unanalyzed, appeared normal showed on retrospect an anterior extension of the sellar fossa which passes like the neck of a gourd under the anterior clinoid processes. Evidences of secondary hypophyseal symptoms were inconspicuous.

Chronic arachnoiditis: The recognition of the presence of tumors in the chiasmal region, such as the suprasellar meningiomas just described, without glandular disturbances and without abnormalities of the sella turcica as seen by X-rays has sometimes led to explorations of this region which disclosed, not a tumor, but a thickening of the arachnoid in the region of the chiasm with pocket-

ing of fluid in leaves of arachnoid membrane partially adherent to each other. What is more, a breaking up of the adhesions has usually resulted in marked improvement of vision and of the visual fields. In retrospect, these patients have often had severe cranial traumata or infections in or near the meninges and brain. They very frequently, while presenting themselves with signs of visual disturbance and visual field defects, do not show the characteristic bitemporal defect so usual in pituitary tumors. The loss of vision is likely to be much more rapid than in the case of cyst or tumor. It has thus been possible to attempt a positive diagnosis of this condition pre-operatively. Heuer and Vail¹⁵ have even gone so far as to suggest that many cases of obscure primary optic atrophy unassociated with syphilis, such as are usually labelled "retrobulbar neuritis of unknown origin," may be examples of the condition under discussion.

Aneurysms of the circle of Willis: A favorite seat for cerebral aneurysms is at the junction of the internal carotid arteries with the anterior or middle cerebral vessels or in some of the other branches of the Willesian circle. It is obvious that a sacular enlargement occurring in this region might present diagnostic difficulties in differentiating it from some of the other lesions already mentioned. However, its frequent proximity to the orbital fissure giving rise to ophthalmoplegia, the frequent occurrence of slight ruptures of its wall, resulting in unconsciousness, meningismus and bloody cerebrospinal fluid, finally the occasional presence of a crescent-like calcium deposit in the wall of the sac demonstrable on the X-ray film, makes the diagnosis possible in the majority of cases. It should be mentioned that unlike aneurysms elsewhere in the body, syphilis is seldom found as an etiological factor, the majority being due to a congenital weakness of the vessel walls or to arteriosclerosis.

TREATMENT

Most of the lesions described are amenable either to alleviation of their symptoms or occasionally to cure by surgical means. Historically, the first operations to be attempted were in cases of pituitary adenoma. A variety of approaches was worked out, many of them consisting of plastic operations through the nose and

mouth. The last of these was the transphenoidal approach used by Cushing and Frazier so brilliantly for a number of years. This type of approach always leads to the exposure of the sella turcica contents from below, and therefore is serviceable only in cases of strictly intrasellar adenomas. Now since we know that perhaps the majority of adenomas exceed the confines of the sella and that most of the other lesions with which the adenomas, especially not associated with acromegaly, may be confused, are either partially or wholly located above the sella, the tendency has grown to approach all the lesions in the neighborhood of the chiasm through craniotomy. The lesion may be reached by lifting the frontal lobe anteriorly or the frontal and temporal lobes laterally. In either case, it is one of the most difficult operations in neuro-surgery since at best the depth at which the lesion is located is considerable and the field small, and the tissue under the operator's retractor, soft, easily injured brain. In the case of an adenoma which cannot be completely removed for fear of destroying the entire pituitary organ, only enough is taken out to relieve pressure upon the optic nerves and chiasm. After this, the growth may be controlled by radio-therapy. In some cases, therefore, where the diagnosis of adenoma can be made with assurance, as for example in acromegaly, and the vision is not imminently threatened, radium or deep X-ray therapy may be undertaken without preceding operation, and often with very satisfactory results. Not only the headaches and impairment of vision may improve as a result of the operation, radio-therapy, or both, but the glandular disturbance may show signs of improvement.

Unfortunately adenomas of the pituitary are the only primary lesions in this region that are radio-sensitive.

The craniopharyngeal pouch cysts are eminently unfavorable lesions from the point of view of therapy which can only be of a surgical nature. Because of their congenital origin, histologically benign character, and slow growth, they are almost always well entrenched by tight adhesions and calcium formation, so that after the cyst content is emptied, the walls can very seldom be removed without endangering the life of the patient. On the other hand, failure to remove the cyst wall invariably results in refilling of the

cyst with progression of symptoms to blindness and eventually death. However, because of the rare occasions, especially in young children when the cyst can be removed and those cases where in spite of only partial extirpation, the regrowth takes place slowly over a number of years, we still valiantly attack these lesions with the constant hope that the patient in hand may be one of the fortunate ones.

The situation is quite different when dealing with the suprasellar meningiomas. These lesions are usually quite small, weighing from 8 to 10 or 10 to 15 grams. They arise from the meninges over the tuberculum sellae to which they are adherent. It is now possible by use of an electric loop to cut away, quite bloodlessly, the adherent area piece-meal, after which it is a relatively easy matter to tilt out the remaining shell of tumor. Many hardships may stand in the way of accomplishing these desired results, and a fair proportion of patients may succumb to the accidents and incidents of the operative procedure. However, in most cases, the tumor can be removed entirely and often the operation is followed by a gratifying return of visual power.

The gliomas of the chiasm present a gloomy picture again. The tumor usually consists of mature cells which do not yield to the influence of radiation, and surgically, the infiltrating character of the growth, makes its removal impossible without destroying the optic nerves. Undisturbed, the tumor itself slowly destroys these nerves and eventually leads to the patient's death.

The chiasmal symptoms of chronic arachnoiditis may often be cured by tearing out the thickened and adherent membrane. The prognosis should be guarded, however, since these symptoms may be simply local manifestations of a generalized process.

Aneurysms, here as elsewhere, have called forth the ingenuity of surgeons, and a few cases are known which have been cured or at least deactivated by filling the sac with bits of muscle through a tiny needle hole and thus bringing about clotting, or floating a piece of muscle into the sac by putting it into the carotid artery and allowing the blood stream to carry it upward. Essentially, nevertheless, it is also a slowly progressive, inoperable condition, which is exposed only when the diagnosis is uncertain.

SUMMARY

The pituitary gland is a complex organ presiding over the growth of the body, its metabolism and the regulation of function of most of the other endocrine glands.

Its position is in close proximity to the vegetative centers of the hypothalamic region, the optic chiasm and the circle of Willis.

Tumors of the pituitary and its neighboring structures while presenting many symptoms in common vary in their clinical manifestations according to their origin, character, size, position, and direction of growth. By means of these variations most of them can usually be diagnosed clinically. Such accurate diagnoses are important in guiding the plan of treatment.

The treatment is generally of a surgical nature, sometimes in combination with roentgen therapy, although at times the latter alone may be used to advantage.

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THE NERVOUS SYSTEM AND ANTIBODY PRODUCTION

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Review of Literature

The rôle of the nervous system in the production of antibodies in man is still obscure. A conflicting literature reveals on the one hand investigators who, like Pfeiffer,¹ picture antibodies as specific internal secretions resulting from a chemically specific antigen irritation of sensory nerve fibres or nerve endings, and on the other hand those who disclaim the possibility of any such direct relationship between the nervous system and antibody production. Friedberger and Oshikawa² performed the interesting experiment of injecting a minute amount of killed *Proteus* X 19 culture into the ear tissue of a rabbit and then cutting the ear off 10 minutes later. They found a higher agglutinin titer in the animal when the ear had been cut off than when the ear remained intact.

In subsequent papers Friedberger and his colleagues extended their observations³ and failed to find a more marked specificity after the removal of the antigen depot, even when threshold doses were used. By speedy removal of the antigen depot no deleterious influence on the intensity of antibody production was noted. This work was corroborated by Dölter and Kleinschmidt⁴ but they pointed out that Friedberger's procedure did not prevent the antibodies from getting into the circulation and that the degree of clamping of the ear to prevent this access is of utmost importance. These investigators do not exclude the possibility of a nervous influence.

Reitler⁵ brought forward evidence to prove that antibody production was a reflex phenomenon. He showed that the properties of reflex antigenic activity are best brought out by freshly isolated strains of bacteria and that two short speedily successive antigenic stimuli worked in association. When the stimuli were complex, a repetition of the first stimulus alone, brought about a rapid rise in antibody titer of both. When the second stimulus was applied there was a tardy increase in antibodies to the first stimulus and

little or none in the second. Reitler very interestingly draws the analogy to psychologic association patterns and claims that in antibody production we are observing a general physiologic law. Belak⁶ and his associates studied the problem from a different point of view. They found that the repeated daily administration of a small dose of pilocarpin simultaneously with paratyphoid-B bacilli subcutaneously or intravenously caused a marked rise in titer in rabbits as compared with animals receiving atropin or distilled water simultaneously with an injection of bacilli. With the same technic 0.5 c.c. of physiologic saline also caused a rise in titer. Adrenalin and thyroxin on the contrary inhibited antibody production. Moreover, Siegler⁷ has shown that cold diminishes the nervous response to antigen. Rabbits' ears were warmed or chilled for 20 to 30 minutes prior to injection with paratyphoid-B bacilli. They were cut off immediately after the injection. The agglutinin titer of the animals was markedly lower in those having chilled rather than warmed ears.

The outstanding positive contributions in this field are those of Metalnikov who has recently summarized his results.⁸ In a series of studies with guinea pigs and rabbits he has shown that by following Pavlov's conditioned reflex procedure he could elicit a rise in antibodies with conditioning stimuli alone. This was accompanied by a leucocytosis. His method was to inject dead bacilli daily for 15 days into the experimental animals after a preliminary excitation with a hot metal plate to the ear for 1 or 2 minutes, ringing a bell, or scratching the flank. After a rest period of 2 to 3 weeks the animals received the thermal, auditory, or tactile stimulus alone without the injection of micro-organisms. A rise in antibodies was observed while control animals showed no such rise.

Vigodchikoff and Barykina⁹ used a thermal stimulus (a heated metal plate) and bouillon as an antigen for 21 days in guinea pigs. Control animals were not given the thermal stimulus. Twelve days later the conditioned animals received the thermal stimulus alone, while the control animals received an injection of bouillon. Forty-one animals were included in this study. The peritoneal exudate was examined in all instances and the cellular reaction found to

be identical in both series which were markedly higher than in normal controls. In other words with a conditioning stimulus alone the cellular reaction was as great as that obtained by the injection of antigen. The cellular reaction is of fundamental importance in immunity as the authors point out. Similar results were obtained by Ostrovskaya¹⁰ using practically the same methods. When the experiment was repeated with 12 rabbits using typhoid vaccine injections following thermal, auditory and tactile stimuli a rise in agglutinin titer was induced by the conditioning stimuli alone. However, it is very important to note that when the same conditioning stimuli were given to control animals which had received only typhoid vaccine, the agglutinins also increased. This throws considerable doubt on the thesis that the conditioned reflex influences antibody production. Podkopaieff and Saatchian¹¹ injecting heated *Staphylococcus* suspensions in rabbits arrived at the conclusion that: "the influence of the conditioned reflex on the cellular reaction in immunity is an incontestable fact. We believe that this demonstration should be of great importance to clinical medicine."

In a series of experiments with rabbits and guinea pigs in which they adhered closely to Metalnikov's methods, Nicolau and Antinescu-Dimitriu¹² reported an increase in titer from 1:600 to 1:1800 with the thermal and tactile stimuli alone and a rise from only 1:600 to 1:800 in the control. With an auditory stimulus the titer rose from 500 to 600 and in the control from 300 to 400. They also noted a hyperleucocytosis (10,000 to 15,000) with an augmentation of "pseudoeosinophiles" at the expense of lymphocytes in treated animals, thus confirming Metalnikov's⁶ findings. Using intraperitoneal injections of tapioca and the "grass" bacillus they again found that the blood picture was modified in properly conditioned animals. However, similar changes were observed in controls. This indicates that the leucocytosis if not within normal limits of variation was due to the prick of the needle and not to the conditioned reflex pattern.

Polletini¹³ using typhoid vaccine in rabbits confirmed Metalnikov's conclusions. Incidentally this author failed to induce anaphylaxis by conditioned reflex.

Glutowa¹⁴ concluded that physical factors such as sunlight, electricity, salt, faradic currents, etc., increased the titers of animals and of man previously injected with typhoid vaccine. This does not conflict with Metalnikov's notion of the influence of nerve centers on immunologic reactions. Conradi and Bieling¹⁵ have pointed out that other infectious agents cause a rise in titer in animals immunized to *B. typhosus*. Cruveilheir, Nicolau and Kopcionska¹⁶ reported that when rabies virus was injected simultaneously with typhoid vaccine there was a markedly higher titer than when typhoid vaccine was injected alone. Felix¹⁷ has shown that agglutinins existing as a result of previous typhoid inoculation may be stimulated non-specifically by the introduction of living bacilli, formolized, or phenolized organisms.

Having considered the evidence in support of the contention that the nervous system plays an important rôle in the production of antibodies it becomes necessary to summarize the investigations which are opposed to this view. Cohn¹⁸ basing his conclusions on anaphylaxis produced by horse serum in guinea pigs, stated that sensitization could only be effected through circulation, that is, only when there was a possibility of antigen resorption. Other tissue elements (skin, muscle, nerve, bone or arteries) were in no way associated with the production of antibodies.

In a recent communication Roberts¹⁹ has shown that a single injection of a minute amount of antigen stimulates the production of antibodies. In spite of rapid extirpation of the antigen depot, Roberts established the fact that antigen is nevertheless immediately transported by the veins and that the mechanism is not a reflex-like process nor is it due to the activity of the nervous system.

The most devastating criticism of Metalnikov's work is to be found in a paper by Friedberger and Gurwitz.²⁰ It will be remembered that Friedberger and his associates were among the first to be intrigued by the possibility that Pavlov's work with the conditioned reflex might be extended to immunology. However, upon repeating Metalnikov's⁸ procedure Friedberger and Gurwitz²⁰ draw attention to the fact that the daily fluctuation in titer of the experimental animals was large enough to account for any rise

apparently due to conditioning alone. They also stressed the lack of a sufficient number of control animals in Metalnikov's experiments.⁸ According to their results expressed in averages there was no significant rise in titer in conditioned animals as compared with an adequate number of controls.

Metalnikov has replied to these criticisms, contending that Friedberger and Gurwitz²⁰ failed to follow the Pavlov technic strictly or take into account the importance of positive results in individual animals.²¹

Monari and Gelli²² also repeated Metalnikov's procedure with guinea pigs but found no increase in peritoneal leucocytes. Their conclusions therefore were diametrically opposed to those of Metalnikov.⁸ Ramon and Zoeller²³ appreciating the fact that they were using an insufficient number of injections failed to observe any rise in titer when using one of two anatoxins that had previously been injected simultaneously.

According to Ramon²⁴ in horses previously immunized against diphtheria toxin, subsequent immunization against tetanus toxin failed to elevate the titer against diphtheria and diphtheria toxin itself is necessary to produce such a rise in titer.

The only important investigation of the conditioned reflex in relation to immune responses in man is that of Lobatch²⁵ quoted by Metalnikov.⁸ Using 6 normals, 14 general paralytics, 11 schizophrenics, 4 oligophrenics and 1 epileptic he made 186 tests. His conclusions were as follows:

1. Leucocytosis accompanies not only the taking of food but also the sight of food.
2. The leucocytic reflex can be provoked equally well by the environmental setting while taking food.
3. The leucocytic reflex is produced after a latency period of 5 to 15 minutes.
4. The number of leucocytes found as a result of a conditioned leucocytic reflex may exceed the number of leucocytes ordinarily present during the consumption of food.
5. Among persons of high alimentary excitability such as oligophrenics and certain general paralytics the manifestation of the conditioned leucocytic reflex is particularly striking, the leucocytic

count being double or even more than double the number of leucocytes ordinarily present.

Plan of Investigation

From our review of the literature it is at once apparent that there is a wide divergence of opinion as to the rôle of the nervous system in antibody production. Because of the complexity of the problem it is not surprising that practically all experimentation has been confined to rabbits and guinea pigs. If such a phenomenon as that described by Metalnikov⁸ could be elicited in man it would be of tremendous importance in understanding immune responses and also in interpreting psychologic patterns. Motivated by such considerations the following investigation was undertaken: Neurotic and psychotic patients in our hospital were conditioned for 21 consecutive days at exactly the same hour and under exactly the same environmental conditions to a thermal stimulus, i. e., an ice-cube applied to the right cheek bone, followed by a subcutaneous injection of a small dose of typhoid vaccine kindly supplied by the New York City Board of Health. After 21 injections by the same operator a rest period of about 2 weeks followed. Titers were measured weekly and when they fell consistently the subjects were given the thermal and tactile conditioning stimuli: (ice-cube and needle-prick—with or without saline) in the original setting. Four experiments have been performed and the results may best be given in chronological order.

First Experiment

In the first experiment 6 psychoneurotic patients received 0.1 c.c. of diluted typhoid vaccine for 21 days and 6 more received 0.1 c.c. saline only, following a sharp blast on a police whistle. The number of dead typhoid bacilli was so small that it had to be increased quite sharply before a demonstrable titer was forthcoming. The titer continued to rise during the rest period following the 21 typhoid injections so that the experimental injection of saline in those patients was delayed until 35 days later. At that time the conditioning stimuli were given 3 times each day for 2 successive days and at 9 a. m. the third day. Blood was taken one hour later

and in 2 patients out of 6 there was a rise in titer from 1:200 to 1:250. The patients injected daily with saline were uniformly negative throughout. During the 21-day period differential blood counts were made on all patients and there was no essential change, although Metalnikov claims to have observed a lymphocytosis in animals similarly treated with killed cholera vibrios.

Second Experiment

Because of the slight rise in titer in 2 out of 6 patients a second experiment was undertaken. The subjects were of both sexes and ranged from 16 to 49 years of age. Four were psychoneurotic, 2 were diagnosed dementia præcox and 5 manic-depressive. Only patients who had never had typhoid fever or vaccine were selected for our studies. Each received 21 daily injections of typhoid vaccine following the application of an ice-cube to the cheek bone for 10 seconds. The patients were divided into 3 equal groups, each group receiving a different number of dead typhoid bacilli, i. e., 50,000, 100,000 and 500,000 respectively. Ten days after the last of the 21 typhoid vaccine injections the titers were on the down grade as determined by bleedings on that day and 4 days later. On the 15th day of the rest period all patients received the stimulus of an ice-cube and an injection of 0.1 c.c. sterile physiologic saline under the original conditions. This was repeated 15 minutes later. A blood examination for agglutinin titer was made 75 minutes later.

The results are recorded in Table 1.

Of the 11 patients (one discontinued voluntarily) so tested, 6 showed a rise in titer of 1 dilution step (i. e., the increment of difference between successive dilutions in geometric progression); one a rise of 2 dilution steps; and one a rise of 3 dilution steps. Three showed no change. It would appear that an immunologic response was elicited in three-fourths of the conditioned subjects by the injection of saline. Twenty-four hours later the blood examination showed a marked decrease in titer in all subjects. There was a drop of 1 dilution step in 4 subjects; a drop of 2 dilution steps in 1 subject; a drop of 3 dilution steps in 1 subject; and a drop of 4 dilution steps in 1 subject. Forty-eight hours after the

TABLE 1. RESULTS OF SECOND EXPERIMENT

No.	Typhoid bacilli per 0.1 c.c.	Titer before procedure	Titer 75 min. after Injection	Rise of titer (in dilution steps)	Titer 24 hours after saline	Titer 75 min. after distilled water Injection	Rise of titer (in dilution steps)	Titer 20 hours after distilled water	Titer 75 min. after conditioning Injection	Titer 3 days after conditioning	Titer 75 min. after conditioning Injection	Titer 1 day after conditioning	Titer 75 min. after vaccine without conditioning 2 days later
1	50,000	1:20	1:40	1.0	1:20	1:40	1.0	1:20	1:20	1:20	1:20		1:40
2	50,000	1:20	1:40	1.0	1:20	1:40	1.0	1:80	1:40	1:40	1:40		1:40
3	50,000	1:40	1:60	2.0	1:20	1:80	2.0	1:80	1:80	1:80	1:160	1:80	1:80
4	50,000	1:40	1:80	1.0	0	1:80	3.0	1:80	1:80	1:80	1:40		1:80
5	100,000	1:20	0	0	1:20	1:20	0	0	0	0	1:20	1:20	1:20
6	100,000	1:40	1:320	3.0	1:20	1:160	3.0	1:80	1:160	1:80	1:160	1:80	1:160
7	100,000	1:80	1:160	1.0	1:40	0	0	1:160	1:80	1:80	1:160	1:40	1:80
8	100,000	1:40	1:40	0	1:20	1:40	1.0	1:80	1:40	1:20	1:20		1:40
9	503,000	1:40	1:40	0	1:20	1:40	1.0	1:40	1:40	1:40	1:80	1:40	1:20
10	500,000	1:80	1:160	1.0	1:40	1:80	1.0	1:160	1:80	1:80	1:80		1:320
11	500,000	1:320	1:640	1.0	1:160	1:320	1.0	1:320	1:320	1:640	1:640		1:640

injection of saline the subjects were twice given 0.1 c.c. of sterile distilled water following the application of an ice-cube. Seventy-five minutes later the blood examinations showed a rise in titer of 1 dilution step in 6 subjects; 2 dilution steps in one subject; and 3 dilution steps in one subject. This indicated a definite response in titer to distilled water which was approximately the same as that with saline, indicating that the small amount of sodium chloride previously used was of no significance. Twenty hours after the injections of distilled water the titer was lower by one dilution step in 4 subjects; the same in 3; higher by 1 dilution step in 3 subjects; and higher by 4 dilution steps in one subject which had not responded on the previous day.

The same morning the subjects were pricked with a needle attached to a stuffed syringe (no fluid being expelled) following the application of an ice-cube. Only one subject showed a rise in titer. Blood examinations were made three days later on the afternoon of the 22nd day of the rest period. The following morning the patients were subjected again to the last procedure described. Blood taken seventy-five minutes later showed a rise of 1 dilution step in 5 subjects. Twenty-four hours later the titer in 4 of these had decreased 1 dilution step.

On the 24th day after the last of the original 21 typhoid injections all subjects received 0.2 c.c. typhoid vaccine in the scapular region at the hands of their physicians under a different environmental setting, i. e., without conditioning stimuli. Five subjects showed a rise in titer of 1 dilution step and one subject a rise of 2 dilution steps as compared with the last recorded titers.

The second experiment yields evidence of a rise in typhoid titer in previously conditioned subjects when the conditioning stimuli alone are applied. It is important to bear in mind that in both experiments just described the titers were determined by only one observer making a single reading of each tube.

Third Experiment

In order to accumulate further data a third experiment was undertaken. Sixteen patients of both sexes, ranging from 15 to 52 years of age were diagnosed as follows: 4 psychoneurotic; 6 de-

mentia præcox (3 catatonic); 2 manic-depressive; 2 general paralysis; and 2 psychopathic personality without psychosis. The blood group was determined. The transference (in the Freudian sense) to the operator was recorded by two physicians and the operator. Skin reactions following injection were noted. At each blood examination the titer for natural antibodies to the Shiga dysentery bacillus was determined as well as the typhoid titer. All sixteen patients were injected subcutaneously daily with 0.1 c.c. of typhoid vaccine (containing 100,000 dead bacilli) following the application of an ice-cube to the right cheek bone while the operator counted up to 10 audibly. The hour and setting were constant. After 21 daily injections the patients were allowed to rest for 18 days. Blood was examined in the interval in order to watch the curve of the agglutinin titer.

On the 19th day, 8 subjects were thrice given the prick of a needle (attached to a stuffed syringe) following the application of an ice-cube. Blood was taken 75 minutes later. Two subjects remained uninjected as base-line controls. Three subjects received 0.1 c.c. typhoid vaccine three times with conditioning and 3 subjects received 0.3 c.c. typhoid vaccine in the scapular region from a physician in a non-conditioned setting.

Two days later all subjects except the 2 base-line controls and the 3 who received typhoid vaccine without conditioning were given 2 injections of 0.1 c.c. sterile saline following the application of an ice-cube. The results are incorporated in Table 2.

The titers of each subject were read independently by 3 bacteriologists. At least 2 readings were made on each set of tubes by each observer. Two used a 6X magnifier and the other who had made the readings in the two previous experiments used a 10X magnifier. Where the readings of a titer were not identical, the final titer recorded in Table 2 represented the 2 agreeing values.

From the data in Table 2 it will be seen that of the 2 subjects receiving no further injections neither showed any rise in titer. Of the 8 subjects receiving the conditioning stimuli 6 showed a rise in titer of one dilution step and 2 showed a rise of one-half dilution step. Thus we have some slight evidence that in properly con-

ditioned subjects a repetition of the conditioning stimuli alone may yield a rise in titer of typhoid antibodies.

TABLE 2. RESULTS OF THIRD EXPERIMENT

No.	Procedure	Titer before	Titer after	Rise of titer in dilution steps
12	No injections	1:320	1:320	0
13	No injections	1:120	1:120	0
14	Conditioning	0	1: 20	1.0
15	Conditioning	1: 60	1:120	1.0
16	Conditioning	1:160	1:320	1.0
17	Conditioning	1: 40	1: 80	1.0
18	Conditioning	1: 80	1:160	1.0
19	Conditioning	1: 60	1:120	1.0
20	Conditioning	1: 60	1: 80	0.5
21	Conditioning	1: 60	1: 80	0.5
22	Vaccine without conditioning	1: 80	1: 80	0
23	Vaccine without conditioning	1: 40	1:120	1.5
24	Vaccine without conditioning	1: 40	1:120	1.5
25	Vaccine with conditioning	1:120	1:160	0.5
26	Vaccine with conditioning	1: 40	1: 60	0.5
27	Vaccine with conditioning	1: 30	1: 60	1.0

The injection of typhoid vaccine without conditioning caused a rise of one and one-half dilution steps in 2 out of 3 subjects. Typhoid vaccine with conditioning caused a rise of one-half dilution step in 2 subjects and 1 dilution step in the third. It might be expected that vaccine with conditioning would yield higher titers than vaccine without conditioning. The findings might be accounted for by the fact that these subjects received 0.3 c.c. vaccine without conditioning in one dose, while in the group receiving vaccine with conditioning there were 3 doses of 0.1 c.c. each administered.

In general one might be led to infer that the rise in titer from conditioning stimuli alone was approximately equivalent to a single injection of typhoid vaccine of the accustomed dosage. Both Tables 1 and 2 would seem to point in this direction. It is of interest to note that in practically all individuals there was a rise in titer of natural Shiga antibodies paralleling the rise in typhoid

titer during the 21-day injection period but that subsequently the Shiga titer fluctuated within experimental error indicating that the rise and fall in typhoid titer was probably a specific response to the conditioning stimuli. Neither the blood group of the patient nor the transference to the operator had any bearing on the results obtained.

Because of the comparatively small number of cases in these experiments, 39 in all, and the lack of a sufficient number of base-line controls we had great hesitancy in drawing any conclusions. The data, however, seemed worthy of further study at the hands of an expert in the statistical psychological field. Dr. Irving Lorge of Teachers College very generously went over all our data and according to his findings, based on the technic devised by Fisher,²⁶ in which the three observers were differently weighted, there was a rise in titer in subjects receiving conditioning stimuli as compared with their own titers before the stimuli were applied.

FOURTH EXPERIMENT

Because of the equivocal nature of our results it became necessary to repeat the experiment under more rigid conditions. First, it was essential to have an equal number of controls and treated subjects. Secondly, it was imperative to standardize the technic of determining agglutinin titer. Thirdly, it was of paramount importance to conceal the operator's procedure from the observers who read the tubes and to conceal the identity of the patients in the control and treated groups. The fourth experiment was planned with these considerations in mind.

I. LABORATORY TECHNIC

A. *Preparation of Antigen:* Culture—*B. typhosus*—Kindly furnished by Dr. D. Khorazo of the College of Physicians and Surgeons, New York, isolated from a case of typhoid fever in December, 1930. This culture has been maintained on beef extract agar. Before use the culture was transplanted every day for several days to insure rapid growth and was then grown on a beef extract agar surface in Blake bottles for 24 hours. Smears from each bottle were examined by the gram stain to exclude any which showed contamination. After standing in the ice box for 5 days the slants

were washed down with sterile 0.85 per cent saline to which 0.15 per cent formalin had been added. The concentrated bacterial suspensions were stored in the incubator until found to be sterile and were then placed in the ice box. After 21 days they were shaken in the electrical shaking machine for 2 hours. After filtration through Schleicher and Schull filter paper No. 589 the filtrate was diluted with formolized saline to a density corresponding to No. 4 on the McFarland nephelometer scale. The antigens were then distributed in small sterile, rubber-stoppered flasks and stored in the ice box. A quantity of antigen sufficient for the entire experiment was made up. Before use the antigen was diluted with an equal quantity of saline and shaken in the shaking machine for 15 minutes.

New and old antigens were titrated against typhoid antiserum. The new antigen properly diluted yielded a positive titer in 1:6400 dilution. The count was 77,800,000 dead bacilli per c.c.

B. *Blood*: About 2 c.c. of blood were taken from an arm vein into a sterile syringe and delivered into a clean serologic test tube. The tubes were stoppered with corks and kept in an inclined position. On returning to the laboratory the clot in each tube was loosened from the wall by a glass rod or applicator. The tubes were allowed to stand upright for about one hour, after which they were centrifuged at 3,000 revolutions per minute for 10 minutes. The serums were pipetted from the clots with a capillary pipette supplied with a rubber bulb into separate clean serologic test tubes. Numbers were then substituted for the patients' names.

C. *Glassware*: All pipettes and capillaries immediately after use were placed in a container full of water. Test tubes, pipettes and capillaries were soaked in dichromate cleaning mixture overnight thoroughly washed 3 times in running tap water and flushed out twice with distilled water. They were thoroughly dry before using.

D. *Set-Up*: Unsterilized physiologic saline 0.85 per cent made up with double distilled water and carefully filtered was distributed by difference from a 1 c.c. pipette graduated in tenths into a series of 75 x 10 m.m. serologic tubes. These tubes were rigorously selected within a variation in diameter of ± 0.25 m.m. New tubes were used just prior to the experimental procedure. A 0.2 c.c. serologic pipette graduated in hundredths was used to deliver 0.1 c.c. of undiluted patient's serum into the first tube to which 0.9 c.c. saline was then added from a 1.00 c.c. pipette to make a 1:10 dilution. One-tenth c.c. was delivered into another tube and 1.4 c.c. saline added for the 1:15 dilution. The remaining tubes in each set received 0.25 c.c. saline for the subsequent dilutions in geometric progression. Using a

clean 1 c.c. pipette, the first dilution of each set was mixed by drawing up and down 4 times. (One-half c.c. was discarded from the set starting 1:10 and 1 c.c. from the set starting 1:15). Twenty-five hundredths c.c. was then measured and expelled into the next tube of saline and the pipette discarded. This diluting procedure was repeated using a new pipette for each dilution until the desired number of dilutions was made. The last tube in the series was corked and stored in the ice box to be used in case the titers were higher than anticipated.

Typhoid antigen was added by means of a 1 c.c. pipette, delivering 0.25 c.c. by difference. The tubes then contained final dilutions of 1:20, 1:40, 1:80, 1:160, 1:320, etc., 1:30, 1:60, 1:120, 1:240, etc. One to ten dilutions were run whenever the 1:20 dilutions gave a negative reading.

E. *Incubation:* After the tests were set up the tubes were shaken two at a time by striking with the finger and then placed in a water bath at 37.5° C with the contents entirely submerged (the tubes being $\frac{3}{4}$ submerged) for 2 hours. They were then ice-boxed over night. Three negative controls using saline instead of serum were run with each test.

F. *Reading of Test:* After removal from the ice box the following morning, the tubes were read by a Spencer microscopic lamp No. 374 with a clear mazda 150-watt bulb. The tubes were read with a hand magnifier 6X by two observers and with an 8X magnifier by the third, the tubes being slightly tilted and gently shaken. The last tube in a series where particles were visible was regarded as the end-point dilution. *It is important to note that in all our data, end-points and not complete agglutinations are recorded.*

Each tube was read independently 3 times by each of 3 readers and the results recorded *without any consultation* either with her own previous reading or that of any other reader. The three separate readings were then submitted for averaging by a fourth person who was the only one acquainted with the classification of the patients and who requested rereadings when these were necessary.

Blood was always taken at 11:15 a. m. (just before the noon-day meal) unless otherwise stated.

II. EXPERIMENTAL PROCEDURE

The procedure in the fourth experiment was as follows: Of the 26 male patients in our hospital used in this experiment 15 were diagnosed as having dementia præcox (4 hebephrenic, 6 paranoid and 5 catatonic); 5 general paralysis; 1 post-traumatic psychosis;

1 psychoneurosis; and 1 depression. They ranged in age from 15 to 47 the majority being under 30. The blood group of each was determined but this proved to be of only academic interest. Every day for 21 days at 9:45 a. m., the subjects were given a subcutaneous dose of typhoid vaccine in the right forearm after an application of an ice-cube to the right cheek bone for the count of ten. The daily environmental setting was constant. The operator and one subject at a time were seated opposite each other in a "treatment" room. The heavy door was kept closed as was the window. The shade was drawn. The operator's tray always bore the same equipment arranged in the same way. He always wore a white coat. The subjects were always taken in alphabetic order. A nurse opened and closed the door, the subject entered and sat in a chair opposite the operator who said: "Good morning, Mr. ——. How are you this morning?" The right forearm (bared to the elbow before entering the room) was swabbed with a piece of cotton saturated with 70 per cent alcohol. An ice-cube (from an electric refrigerator) was gripped in a piece of gauze and held against the right cheek bone while ten was counted in an audible monotone. Immediately thereafter the ice-cube was tossed into a pitcher and a subcutaneous injection of typhoid vaccine administered. The site of injection was then swabbed with 70 per cent alcohol. The cheek bone and arm were then dried with a towel and the patient departed. The needle was then dipped into a beaker of 70 per cent alcohol and the tuberculin syringe filled with vaccine while the subjects were outside the room. They were not informed as to the nature or number of injections.

For the first 3 days the subjects received 500,000 dead typhoid bacilli daily. The following 4 days they received 1,000,000 daily. Then for 10 successive days the dose was reduced to 10,000 per day and for the last 4 days to 1,000.

The rationale of this procedure was an endeavor to approximate if possible the curve of interest of the subjects in the procedure with the probable intensity of conditioning, as well as to cause a definite rise and fall in titer. Blood was taken before any injections of typhoid vaccine were begun and weekly thereafter. Blood

was taken from the arm vein throughout this experiment with needles and syringes freshly sterilized.

As stated at the outset we proposed in this experiment to have an equal number of control and treated subjects. Instead of carrying out the crucial test on the same day in all subjects it was decided to first divide them into 3 approximately equal groups, to be tested on the 9th, 12th and 15th day respectively after the last day of the 21 typhoid vaccine injections. The reason for this grouping was to determine if possible the optimum rest period after injection since the time factor might play a very important part in the intensity of the conditioned reflex. Furthermore, on each of the above mentioned days the group was subdivided as equally as possible into controls and treated subjects. The group for each day was paired off on the basis of titer. Thus if 2 subjects had a titer of 1:160 the day before, one subject was placed among the controls, the other among the tested subjects. If 4 subjects had a titer of 1:320 then 2 were placed in each of the 2 groups mentioned, etc.

The procedure on the 9th, 12th and 15th days was identical. At 9 a. m. on each of these days blood was taken from the appropriate subjects. Neither the physician taking the blood nor those assisting him knew which of these were to be controls and which were to be injected. At 9:45 a. m. the subjects to be injected lined up outside the "treatment room." The operator then injected them with 0.1 c.c. sterile saline following the application of the ice-cube to the right cheek bone exactly as had been previously done with typhoid vaccine. This procedure was immediately repeated. When all the subjects had received 2 injections each, they were taken in rotation again and given 2 more injections. This was again repeated. Thus, within 25 minutes, these subjects received 6 injections of 0.1 c.c. sterile saline following the application of an ice-cube to the cheek bone. Blood was taken from them and from the controls exactly one hour later, i. e., at 11:10 a. m. Again blood was taken at 11:10 a. m., 24 and 48 hours later.

Finally, in order to complete the experimental procedure on the 18th day after the last of the 21 typhoid vaccine injections all the subjects available who had served as controls on the 9th, 12 and

15th days were tested with 6 injections of 0.1 c.c. sterile saline as just described.

The conditions under which the tests were read are of considerable importance. In an attempt to attain complete objectivity the tubes were handled as follows. Serum from each subject was set up in two series of dilutions which we may arbitrarily call the "regular" series, i. e., 1:20, 1:40, 1:80, 1:160, 1:320, etc., and the "interpolated" series, i. e., 1:30, 1:60, 1:120, 1:240, 1:480, etc. Blood was taken at 9 and 11 a. m. the first day of the test and both sera from each subject were set up and incubated at the same time. Thus there were 4 series of tubes for each subject. The first tube in each series bore the subject's name. After ice-boxing over night and before the tubes were read the following morning, the name of the subject was erased and a random number substituted by the operator who was not to read the tubes. Each of the 3 readers then independently noted the end-point agglutination in each set of tubes, the interpolated sets being separated from the regular sets of the same subject and all sets in miscellaneous order. Thus there was a check on the accuracy of reading, for the interpolated reading would have to be juxtaposed to the nearest regular reading for any single serum. Each reader submitted her reading without consultation. All sets of tubes were then renumbered twice. This procedure meant that there were 3 independent readings by each of 3 observers on each serum in each of 2 series of dilutions taken one hour before and one hour after the test respectively. The observers had no way of knowing which interpolated series went with which regular series of tubes nor to which subject any set of tubes belonged, to say nothing of whether it was a 9 or 11 a. m. specimen that was being examined.

The majority of titers before the final test were 1:320 (15 out of 26), about half this number were 1:640 and the remainder scattered between 1:40 and 1:960. The previous maximum titers attained by these subjects were as high as 1:1280, the majority being 1:640 or higher. The results of the test are summarized in Table 3. Limitations of space do not permit of detailed data.

TABLE 3. SUMMARY OF FOURTH EXPERIMENT

Titer in dilution step	Reader No. 1		Reader No. 2		Reader No. 3		Average		Average
	Inj. (13)	Cont. (12)	Inj.	Cont.	Inj.	Cont.	Inj. Cont. 9th, 12th, 15th days	Inj. Cont. 18th day	Inj. Cont.
+1	2				2	2			
+ ½	4	5	5	1	3	5	4	2	2
0	6	5	6	9	6	4	8	9	7
- ½	1	2	2	2	1	1	1	1	1
-1					1				
-1½									1

In Table 3 in the first column are enumerated the differences in dilution steps between the 9 a. m. and subsequent highest titer. Thus if a subject's titer was 1:320 at 9 a. m. and at 11 a. m. (1 hour after injection) it was 1:640, the difference would be +1 dilution step. No change is represented by 0. A diminution in titer is shown by a minus sign. The observations of each reader are given in the succeeding vertical columns which are subdivided into "INJ." which represents injected subjects and "CONT." which represents control or uninjected subjects. The averages are given in next to the last vertical column. In the last vertical column are the averages of all 3 observers on the 18th day after the last of the 21 typhoid injections when all the subjects used as controls on the 9th, 12th and 15th days were injected 6 times with 0.1 c.c. of sterile saline.

According to Reader No. 1 (who was most consistent) 2 of the 13 subjects injected on the 9th, 12th and 15th days showed a rise in titer of 1 dilution step, 4 showed a rise of ½ dilution step, 6 were unchanged and 1 diminished ½ dilution step as compared with 12 controls. In the latter, 5 showed a rise of ½ dilution step, 5 were unchanged and 2 were diminished ½ dilution step.

The similarity is striking in comparing the results (averages) of the injected and the control subjects. However, the maximum difference of 1 dilution step occurred three times in the injected group and *never in the control group*. This observer's individual error was ± 0.145 dilution step which multiplied by 4.3 is ± 0.6235 , the experimental error for comparing different groups. It is difficult, therefore, to arrive at a decision as to the significance of the above positive findings.

TABLE 4. THE MEANS AND STANDARD DEVIATIONS FOR THE AVERAGE OF ALL OBSERVATIONS OF ALL OBSERVERS

Injected subjects					Controls		
No. of days after 1st injection of vaccine	Time blood taken in relation to conditioning stimull alone	Mean	Maximum increase of mean	Standard deviation	Mean	Maximum increase of mean	Standard deviation
0		4.41		2.74			
7		8.15		3.58			
14		10.58		3.27			
21	Last injection	10.80		2.28			
27	Rest period	10.61		2.39			
29	1 hour before	9.03		3.54	10.70		1.22
	1 hour after	9.11		3.68	11.11		1.58
30	24 hours after	9.14		3.43	10.90		1.22
31	48 hours after	9.14	0.09	3.00	11.22	0.52	1.14
32	1 hour before	11.20		1.00	10.49		1.87
	1 hour after	11.40		1.18	10.49	0	1.79
33	24 hours after	11.42	0.22	0.95	10.31		1.97
34	48 hours after	11.30		1.41	10.30		2.04
35	1 hour before	10.90		1.22	10.89		1.18
	1 hour after	10.92		1.10	11.11	0.22	1.22
36	24 hours after	10.58		1.10	10.90		1.14
37	48 hours after	11.05	0.15	1.14	10.90		1.14
38	1 hour before	11.07		1.67			
	1 hour after	10.76		1.95			

When the corresponding averages of the 3 observers are scrutinized we note again that there were 4 subjects showing a rise of $\frac{1}{2}$ dilution step in the injected group, and only 2 subjects in the control group. Injecting the controls on the 18th day yielded precisely the same positive results (averages) as the controls on the 15th day. One must conclude that with the meticulous procedure employed our results are empirically negative.

The statistical summary of our data is incorporated in Table 4 where each integer represents one-half of a dilution step.

According to Dr. Lorge "The correlation coefficients of the observers are high, so that in general one can place dependence upon observers and create greater dependence upon an average of all observers. Generalizing from the means and the standard deviations, there can be little doubt that whatever rise in titers is observed is chance and random since the control group averages greater rises in Series I (9th day) than does the experimental group. In the second Series (12th day) there seems to be a slight rise in favor of the typhoid injection but it is not statistically reliable, nor would I think it logical to put too great dependence upon it. For the third series (15th day) the same thing holds."

COMMENT

Why are the results of the above experiment and that of the first experiment negative, while in the second experiment they were decidedly positive and in the third experiment equivocally positive? This important question can be partially answered by stating that the results of the first and second experiments can be disregarded because of the fact that the readings were made by one observer (the least accurate of the 3) and further that this observer was cognizant of the experimental procedure. The third experiment lacked a sufficient number of controls and again the 3 observers were aware of the operator's procedure. It was only in the fourth experiment that the number of controls and injected subjects was practically equal thereby offering a suitable basis of comparison.

At this point it might be well to emphasize one feature of this investigation which is frequently disregarded in the reading of agglutination titers in experiments of the same or different nature.

Specifically we refer to a psychologic factor. It is common knowledge that we see what we wish to see. That this wish is not always conscious has been sufficiently emphasized in the Freudian literature. Particularly in dealing with so delicate a test as the reading of an end-point in agglutination we are confronted with the human frailties of optical equipment, eye strain, general physical condition, fatigability, preconceptions and wishes as to outcome to say nothing of the inherent difficulties of determining an end-point which is transient and obscured by differences in density, color and reaction of the menstruum. Our experiments indicate that knowledge of the treatment which the experimental subject has received may strongly influence the reading of the end-point of agglutinin titer.

It should also be noted that blood for the first 3 experiments was squeezed from the ear lobe or finger into a test tube while in the fourth experiment blood was taken from the ear vein. Obviously, squeezing blood from the ear or finger introduces diluents such as: tissue fluids, lymph, etc., which reduce the accuracy of the final readings.

Since Metalnikov and others have reported positive findings with animals, while with a similar technic we have obtained negative results in human beings, several questions arise. It is admittedly more difficult to elicit a conditioned reflex in adult men and women than in experimental animals. This is due chiefly to greater distractability. Individuals vary greatly in their capacity to become conditioned. It may be that the stimuli were not given with sufficient frequency nor for the optimum number of days. Again, neither the thermal stimulus, the tactile stimulus, nor the immunologic stimulus may have been of the most favorable intensity. Further, the blood may not have been examined at the most suitable times. We have been dealing with a complex phenomenon associated with a host of variable factors. Perhaps our methods are too crude to measure slight positive responses.

The fact that we have dealt solely with subjects mentally diseased may also have an important bearing upon the negative character of our results. To be sure, we employed a miscellaneous group which ran the gamut from psychopathic personality through

psychoneurotic to psychotic but no mentally normal human beings were included in this investigation.

It is impossible to state dogmatically that the conditioned reflex has no influence on agglutinin titer. All that we can safely conclude is that under the conditions of our experimentation with its obvious limitations we have failed to observe a demonstrable rise in agglutinin titer in subjects in whom we have attempted to induce a conditioned reflex pattern.

SUMMARY

1. In an investigation dealing with 65 mentally diseased subjects the attempt was made to induce a conditioned reflex in association with the injection of typhoid vaccine.

2. Empirically and statistically there was no evidence that a conditioned reflex was established nor that if it had been it exerted any influence on agglutinin titer when injected subjects were compared with appropriate controls.

3. There are important psychologic factors which influence the readings of agglutinin titers. These have been minimized by an objective procedure which is described.

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AN INVESTIGATION OF METHODS OF MEASUREMENT OF THE ELECTRICAL PHENOMENA OF THE SKIN*

BY CARNEY LANDIS, PH. D., AND T. W. FORBES, PH. D.**

That the metabolism of psychiatric patients is frequently disturbed and that probable dysfunction of the autonomic nervous system enters into psychopathic disorders is well known. For example, we have the concepts of Jaensch's adrenal and thyroid types: of vagatonia and sympathicotonia, which are frequently referred to in clinical discussion. To date we have no good technique for measuring or testing autonomic activity. Furthermore, metabolic determinations by the gasometric or by gas analysis methods are not only difficult to obtain, but also of questionable validity and value in the case of non-cooperative psychiatric patients.

Neuro-physiological work indicates that it might be possible to perfect a technique of measurement of electrical phenomena of the skin which should afford an index of activity of the sympathetic division of the autonomic system. At the same time, experimental reports, such as those by Lueg and Grassheim (1929), Lueg (1930) and by Sheard and Purdy (1931), offer clinical evidence that certain electrical measures correlate with metabolism.

By the term electrical phenomena of the skin we mean resistance, potential and capacity, and their variations, including the galvanic skin reflex. The neurological aspects of the galvanic skin reflex have been thoroughly investigated but the neurological bases of the other phenomena have not been intensively studied and are known chiefly by inference. Gildemeister (1922), Landis and De Wick (1929), and Landis (1932) called attention to the fact that the galvanic reflex occurred as one of a group of autonomic reflexes such as dilation of the pupil, changes in heart rate, etc. The work of Shilf and Schuberth (1922) and of Sakamoto (1923) on frogs, and of Foa and Peserico (1923), Wang and Lu (1930) and of Richter and Shaw (1930) with cats, has shown that there are cortical, mid-brain and cord centers which *may* be, but are not *necessarily* involved in the galvanic skin reflex and that an intact sympathetic

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chain is *essential* for the galvanic reflex. Richter (1927) has reported the case of a man whose sympathetic chain was apparently severed on one side of his body. Electrical measurements on this case gave results which were in line with the experimental findings upon animals.

There have been fewer studies of the electrical *capacity* of the skin. Saito (1931) has shown that stimulation of the nerve, changes the capacity of the sweat gland membranes in excised preparations, and since Gildemeister, Strohl and others have shown that membrane polarization is the basis of both the apparent resistance to a direct current and the electrical capacity of the skin, it is reasonable to expect a similar relationship exists between skin capacity and nervous control. The clinical studies of Lueg and Grassheim (1929), Lueg (1930) indicate a correlation of electrical skin capacity with endocrine function and dysfunction.

Studies of basic levels of direct current resistance have not been reported as frequently as studies of the galvanic reflex. Richter (1929a) has reported, that in monkeys the plantar resistance becomes very high when the motor and sensory nerves to the feet are cut as well as when the sympathetic fibers alone are sectioned. Further evidence is needed here, but it seems certain that the level of basic resistance, as well as the occurrence of the galvanic reflex, is partially dependent on sympathetic activity.

It, therefore, seems reasonable that a valid, well controlled technique for measurement of the various phases of electrical skin phenomena should give us an index of the activity of the sympathetic nervous system. The possibility that part of the activity thus electrically registered may be the result of cortical activity of the cerebrum rather than a function of sympathetic activity alone should be minimized. Since it is known that cortical activities are greatly reduced with the onset of sleep, the sleep state provides a condition in which cerebral activity is at a minimum. On this assumption, measures of electrical skin phenomena during sleep should yield an index of sympathetic activity with the influence of cerebral centers reduced and perhaps eliminated, while the same measures taken during waking hours should be influenced by cerebral control. Richter (1926, 1929, 1930) has already reported

finding differences of basic resistance level between sleep and waking states.

In order to develop such a technique of measurement we cannot expect to use at *random* one of a complicated series of inter-acting factors without careful study of inter-relationship and variables to be controlled. The complexity of the problem is indicated by the fact that in the literature of approximately five hundred papers on electrical skin phenomena there are at least a dozen *fundamentally* different methods of measurement represented. Table 1, gives a brief outline of techniques employed to date. We will not attempt here to go into technical details but wish simply to indicate the wide variety of techniques which have been used in order to show the necessity and importance of a systematic comparison and standardization of method of measurement before there can be any hope of agreement on results.

TABLE 1. METHOD OF MEASUREMENT*

Without exosomatic current:

(Measurement of skin potential and reflex)

1. Opposing potentials. (Purdy and Sheard)
2. Direct measurement. (Thouless)

With exosomatic current:

D. C. Resistance and (or) galvanic reflex

No standard current

3. Ordinary Wheatstone bridge—(Féré, Wechsler)
4. Subject in series with galvanometer (Veraguth)

Standard current:

5. Wheatstone bridge (Darrow)
6. String galvanometer (Richter)
7. Vacuum tube set-up (Davis)
8. Pulse of very short duration. (Strohl)

A. C. resistance and (or) capacity

Bridge methods

9. Fixed frequency. (Lueg and Grassheim)
10. Varying frequency. (Gildemeister, Strohl, et al.)

Direct measure

11. Vacuum tube. (Hathaway)

Capacity

12. D. C. break kick-back. (Regelsberger)

Current diffusion

13. Surface path of moist gauze. (Ebbecke)

* The names used to identify techniques do not, of course, form a comprehensive list.

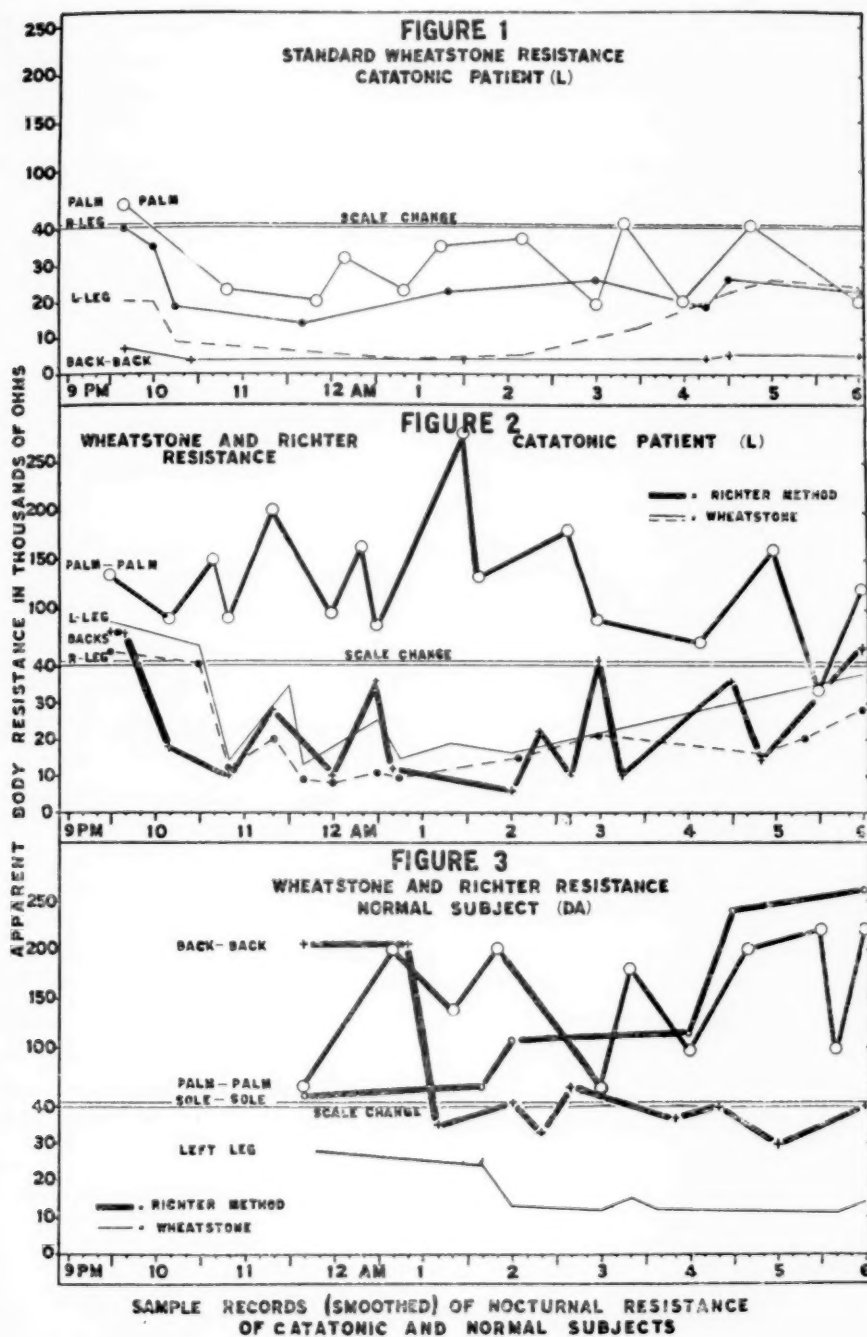
PRESENT STUDY

We have begun such a systematic comparison of techniques during the past year in connection with a study of the sleep of catatonics. Our investigation has taken the form of determination of basic resistance curves during from 6 to 9 hours of the normal nocturnal sleep period on catatonic dementia præcox patients and on normals. We have used the ordinary direct current Wheatstone bridge method and Richter's method in which the resistance is determined by the use of a very small constant current (2 to 4 microamperes) and a varying potential. We have applied electrodes simultaneously to four parts of the body, two of which were sweat gland areas (palms or soles) and two non-sweat gland (lower leg and backs of hands). Parallel readings were taken with each set of electrodes. We have also compared several different types of electrodes.

RESULTS

(A) Curves of resistance during sleep as determined by the ordinary Wheatstone bridge method often differ markedly in form, and *regularly* differ in actual resistance level from those which are obtained by Richter's method. The Wheatstone resistance lies in the region between 5,000 and 40,000 ohms while that obtained by Richter's method falls roughly between 40,000 and 200,000 ohms. The ordinary Wheatstone method uses about 700 times the voltage (0.7 volt) that Richter's method does (1 millivolt), and the applied potential varies with the patient's body resistance. Since it is well known that the amount of potential applied changes the apparent resistance due to polarization, etc., these results are in line with previous physiological work.

Furthermore, curves of resistance obtained by either technique from different body areas having similar sweat gland distribution, such as the soles of the feet and the palms of the hands, often are quite dissimilar. Such disparity is in line with the statement of Kuntz (1929) that the sympathetic innervation to the upper and lower members is centered in different sections of the cord, and with the findings of different rates of sweat secretion of palms and soles by Kuno and Ikeuchi (1927).



Figures 1, 2 and 3 are sample graphic representations of three of our records, picked to illustrate the above points. Figure 1, shows the variations of ordinary Wheatstone bridge resistance for different parts of the body during the period between 9:40 p. m. and 6 a. m. in the case of a catatonic patient. The points illustrated are that—

- (1) The highest resistance level is from 30,000 to 40,000 ohms.
- (2) The resistances of the backs of the hands, the legs and the palms are of differing magnitudes and vary independently in this case.

Figure 2 gives resistance curves of the same nature from the same patient as in figure 1, but determined by different measuring techniques, i. e., by ordinary Wheatstone and by Richter's method. It will be noted that—

- (1) Although the Wheatstone resistances again fall under 30,000 ohms as in figure 1, the Richter measures (which are plotted on the second scale at the left margin) rise as high as 200,000 ohms. This illustrates the different resistance values obtained from the two methods of measurement.

- (2) The resistances obtained by the use of the two methods vary independently.

- (3) The back-back of hand resistance apparently varies independently from the palm-palm when measured by the Richter method.

Figure 3 illustrates resistance levels of a normal subject. The Wheatstone resistance of the leg is, as in figure 2, less than 30,000 ohms while the readings by Richter's method run as high as 200,000 ohms. Other records, not shown here, indicate that Wheatstone measurements from the palms are also not comparable to those made by Richter's method on this same area. Again the resistance curves for the palms, the backs of the hands and the soles of the feet follow independent courses.

Our results clearly indicate that electrical skin resistance and galvanic skin reflex determinations cannot be assumed to be comparable or even to follow a similar course of variation unless identical procedures have been used; or until physical and physiological

factors have been considered, and until techniques have been checked against each other.

(B) The zinc-zinc sulfate electrode has proved most convenient and satisfactory for long continued application.

(C) The ordinary Wheatstone bridge D. C. method using a one and one-half volt source, shows very little variation of basic resistance with catatonic patients. Likewise with onset of sleep which might indicate changing conditions of the sympathetic nervous system little variation is shown. This agrees with previous findings of Landis (1927).

(D) Richter's technique shows a much greater range and frequency in the variation of this apparent ohmic resistance than does the Wheatstone bridge method.

SUMMARY

We have shown that it is reasonable to expect from the nerve sectioning studies on resistance of the skin and on the galvanic reflex, that a valid, standard technique can be worked out to give an index of sympathetic nerve reactivity, but that a systematic study of techniques and of the relationship between measures is a necessary first step toward such a measure if it is to be valid. Our experimental results indicate that curves for basic resistance vary with location of skin area and with technique used. Measurements with an ordinary standard Wheatstone bridge and a source of $1\frac{1}{2}$ volts gave no indication of a relationship to the functions under nervous control. Richter's technique was apparently more sensitive in that it shows a greater range of variation, though we are not yet satisfied as to the exact nature of the electrical phenomena which the technique measures. We plan to make a more extensive study with simultaneous measures and to use still other techniques.

In closing we wish to stress two points which we have raised in this paper. First, that resistance and galvanic reflex curves from differing techniques cannot be *assumed* to be comparable until *shown* to be so; and second, previous experimental and clinical studies, indicate that valid measures of electrical skin phenomena when developed should provide valuable indices of neurological and physiological functions.

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EXPERIMENTAL TOXIC APPROACH TO MENTAL DISEASES
(*The Reaction of the Brain Tissue to Subcutaneous Injection of
Enterogenous Toxic Substances—Indol and Histamin*)

PART II

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IV. EXPERIMENTAL WORK

Our experimental work has consisted of establishing the reaction of the central nervous tissue and particularly of the brain to the influence of two of the most important enterogenous toxic substances which have been discussed in the first part of this paper, i. e., histamin and indol.

We have found very little in the literature concerning the systematic poisoning of animals with small doses of indol or histamin protracted over long periods of time. Only brief mention of the changes found in acute poisoning with indol is made by Herter who reports them as congestion, softening of the brain, edema, and excessive chromatolysis of the cortical nerve cells.

Buscaino⁸⁵ in 1922 reports two cases of experimental histamin poisoning in rabbits in which histologically he found grape-like areas of disintegration and vacuolization of nerve cells especially in the basal ganglia and mesencephalon.

In 1930 Ugurgieri⁸⁶ reported his investigation on the reaction of the oligodendroglia and microglia to histamin poisoning and stated that the oligodendroglia cells react by acute swelling, whereas, the microglia appears normal following a total administration of 366 mg. of the drug in 21 days to a rabbit weighing 2,220 grams.

C. E. Roberti in 1931⁸⁷ injected also a few rabbits with histamin, one animal receiving three doses of 5 mg. another two doses of 8 mg., a third five doses of 10 mg., a fourth ten doses of 10 mg., and a fifth receiving 15 doses of 30 mg. each. The first two animals showed practically no pathology of the nervous system. The third and fourth animals disclosed nerve cells undergoing the severe type of degeneration of Nissl especially in the basal ganglia and

medulla. The Purkinje element also suffered considerably. The reaction of the astrocytes was very slight. A few hypertrophic elements with residual nuclei were seen. There was increased satellitosis about the nerve cells. The blood vessels were congested but the walls were normal. There was slight proliferation of the connective tissue of the blood vessels in the pia.

A rabbit receiving a total dose of 731 mg. showed some cells with deeply stained nuclei and very few Nissl bodies, while other cells showed marked vacuolization.

No other data available in the literature have been found and we, therefore, thought it advisable and of particular interest to check up on the above-mentioned information and extend our investigation to the reaction of the brain tissue in acute, sub-acute, and chronic stages of indol as well as of histamin intoxication.

Because of the fact that the various toxic substances of enterogenous origin are never isolated in the gastrointestinal tract but always associated, we thought it advisable also to detect the toxic effect of more than one substance injected at a time and, therefore, we have investigated the reaction of the nervous tissue to the simultaneous poisoning with histamin and indol.

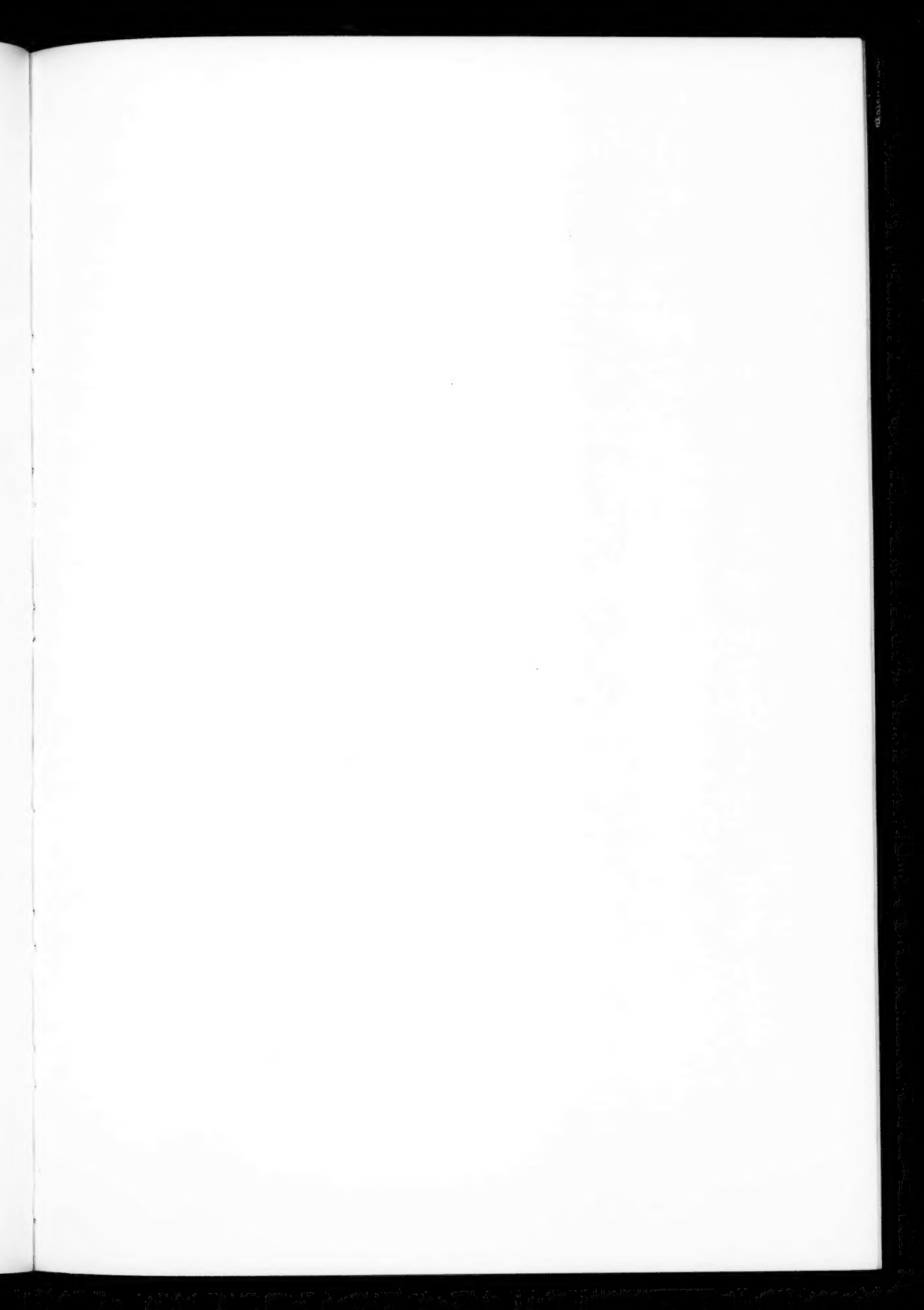
We feel that this attempt of combination of more than one drug is a very important step of our investigation because it deals with actual facts occurring in the gastrointestinal tract where several toxic agents are present at the same time.

Because of the importance of the oxidizing power of the cells, especially of the cells of the liver in detoxifying indol and probably in part, at least, histamin, we have investigated the action of the indol and histamin over the central nervous system while the animals were under the action of a simultaneous administration of potassium cyanide, a drug which is known to be an agent decreasing the oxidizing power of living cells.

A. EXPERIMENTAL INDOL POISONING

Cat No. 1—Lab. 12. Weight 21½ kg.

Animal given one subcutaneous injection of one gram of indol dissolved in 2 c.c. of olive oil. Following the injection the animal showed some twitching which increased and became generalized before the animal was



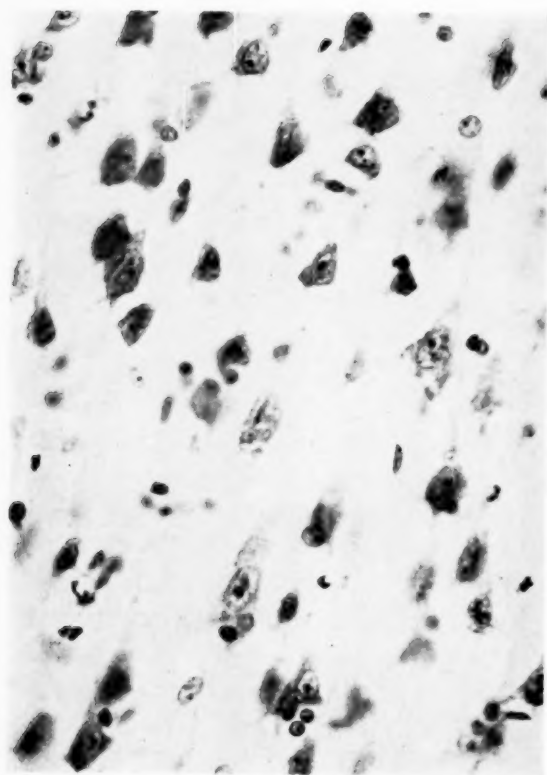


Fig. 1. Slight process of vacuolization in some of the cortical nerve cells. Nissl stain in celloidin sections

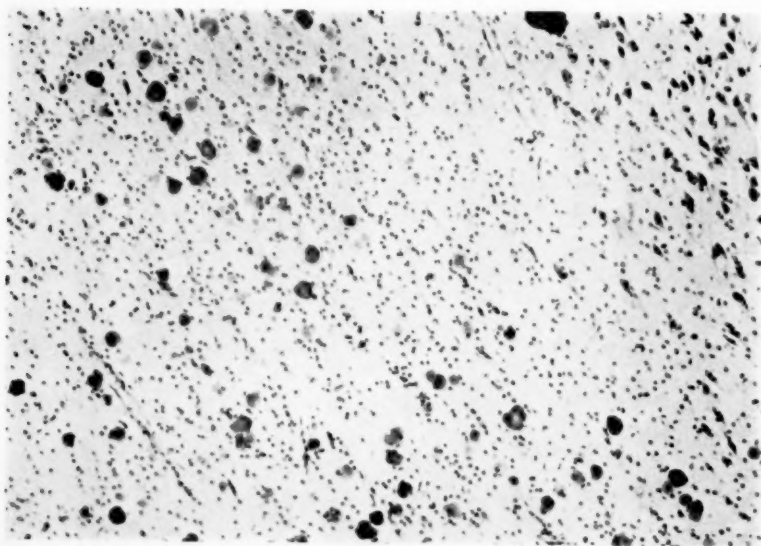


Fig. 2. Metachromatic bodies scattered in the white substance. Nissl stain for nerve cells

killed, increased respiration, general prostration, and indicanuria. The animal was killed 24 hours later. At autopsy half of the brain was fixed in alcohol and embedded in celloidin and serially cut for Nissl stain. The remaining half was used for formol and formol bromide fixation and used for study of neuroglia (astrocytes and oligodendroglia), microglia, nerve fibers, myelin sheaths and fat products of degeneration.

Histological Study: The meninges show no appreciable changes except slight congestion of the blood vessels. In the various cortical areas which have been examined in serial sections the nerve cells do not show appreciable changes though here and there a few elements are found disclosing paleness of the cytoplasm, moderate vacuolization surrounding the nucleus, and occasionally disintegration of the element. It must be mentioned, however, that the comparison of our slides with sections of a normal cat disclose that occasionally pathological changes are also seen in the normal animals involving scattered nerve cells which appear more or less swollen and disintegrated.

The study of the microglia and oligodendroglia as well as the study of the astrocytes reveal no appreciable changes. No pathological changes are detectable either in the white or gray matter of the spinal cord.

Cat No. 2—Lab. 13. Weight $2\frac{1}{2}$ kg.

Animal received two subcutaneous injections of 0.5 grams each of indol at intervals of 24 hours. Animal died 24 hours after the second injection. From the clinical standpoint the symptoms were of the same type as mentioned in Cat No. 1. There was also, as for Cat No. 1, a marked indican reaction in the urine.

Histological Study: The cortex reveals diffuse degenerative changes of the nerve cells of a moderate degree and consisting in slight process of chromatolysis following which the nerve cells involved show granular bodies in the cytoplasm. There is a diffuse paleness of the cells and only occasionally vacuoles surrounding the centrally located nucleus (Fig. 1) are found in some of the nerve cells. The lesions though of a moderate degree are slightly more pronounced in the frontal cortex where they seem to involve most of the cortical layers. In the motor and sensory cortex the lesion seems slightly more pronounced in the external layers of the cortex, first, second, and part of the third layers.

The subcortical formations, the corpus striatum, and thalamus show the presence of various cells with slight degenerative changes. In the hypothalamic region the lesions are slightly more pronounced. The slight changes involving the nerve cells are spread all over the brain stem and in the

cerebellum a slight degree of homogenization of the Purkinje cells, paleness of the cell and pronounced satellitosis is detectable all over. In the granular layers there is a slight tendency towards collection of the granules into more or less large clumps, but no definite conglutination is appreciable.

A common occurrence seems to us the existence of rather diffuse degenerative changes which are detectable with the thionin stain in the glia nuclei surrounding the nerve cells, the so-called satellite cells. The changes consist mainly in the presence of shrinkage of the nucleus which appears deeply stained, the chromatin substance having a tendency to fuse together, the whole nucleus appearing to be undergoing a process of karyorrhexis. This process of karyorrhexis is present to a certain degree in the normal animal but here the extent of the process is evidently greater and is detectable not only in the cortex but also in the basal ganglia.

In the white substance there is diffusion of small areas of metachromatic substance, the origin of which might have something to do with chemical degenerative changes brought by the action of indol (Fig. 2), though not specific for such a substance. This metachromatic substance sometimes invades the gray matter and occasionally seems to be present in some of the glia nuclei. This metachromatic substance having quite often a roundish appearance is also found in some of the blood vessels of the cortex and surrounding these blood vessels the lesion of the nerve cells appears to be more pronounced. It must be mentioned here that a certain amount of such metachromatic changes are occasionally found in a normal brain. The question arises if those brains have to be considered absolutely normal.

The small blood vessels of the cortex disclose a very slight swelling of the lining endothelium and occasionally degenerative changes of their nuclei.

With appropriate stain the astrocytes appear only slightly pathological, the changes consisting in a slight amount of swelling of the cytoplasm, its granular disintegration, and clasmatodendrosis which is present in only groups of cells (Fig. 3). The changes are slightly more pronounced in the region of the hypothalamus and diencephalon.

The silver carbonate method of Hortega as modified by Globus and Penfield discloses a very moderate degree of acute swelling of the oligodendroglia in both white and gray matter. Conversely, the microglia does not show appreciable changes, most of the elements appearing normal in size.

Cat No. 3—Lab. 14.

Daily injection of 0.25 grams of indol. Animal died 24 hours after third injection.

The general pathological changes of the nerve cells do not greatly vary

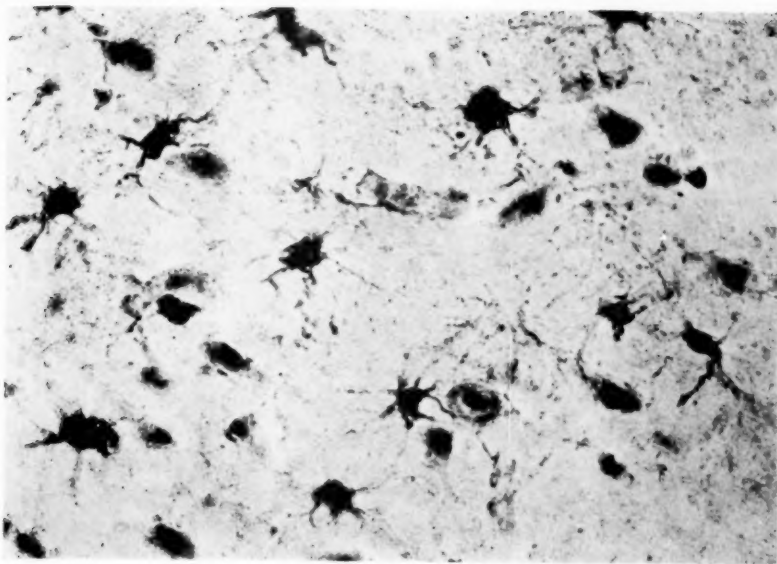


Fig. 3. Slight pathological changes of astrocytes. Cajal gold sublimate method

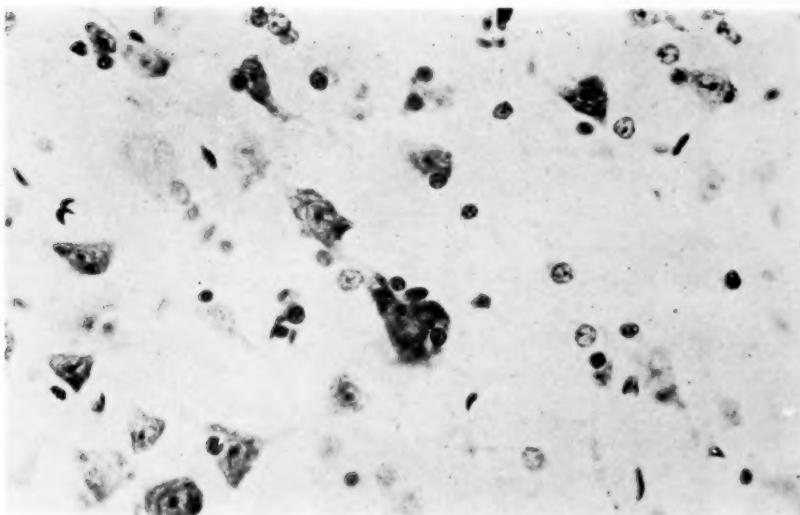
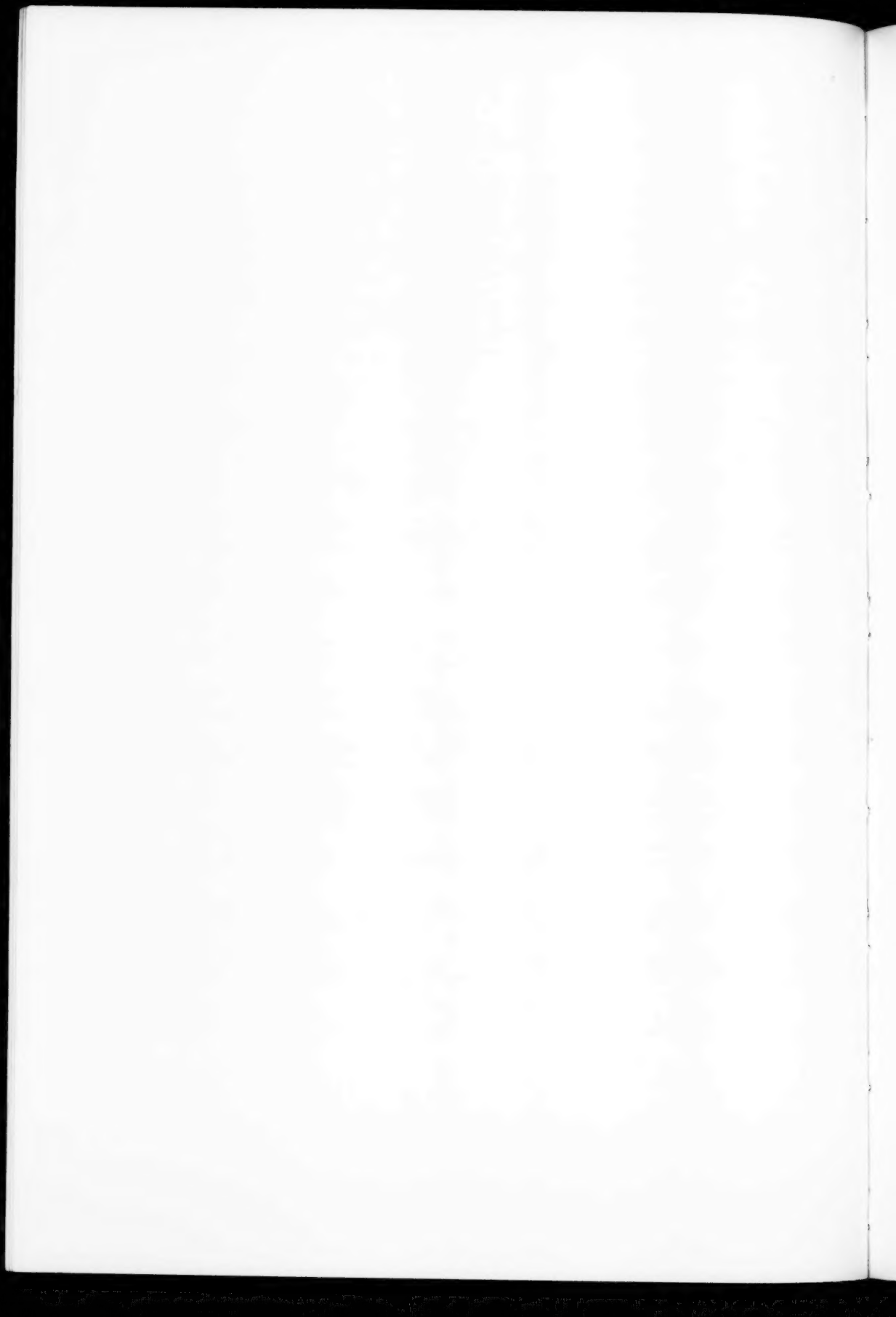


Fig. 4. Fading of nerve cells leading to the formation of acellular areas. Nissl stain for nerve cells



from those in Cat No. 2 and they consist mainly in slight degenerative changes of the nerve cells represented by chromatolysis of the cytoplasm and some granular disintegration of the nucleus. Marked satellitosis is found especially in areas where nerve cells have faded out. This granular aspect is at times evident also in the cytoplasm. The degenerative changes are here also slightly more pronounced in the frontal areas, in the diencephalon, and the temporal lobes. They extend also to the cerebellum where Purkinje elements are found in a stage of homogenization with a tendency towards conglutination of the granular layer. In the brain stem and medulla oblongata diffuse degenerative changes of cells are found, though not pronounced. In the spinal cord a few elements of the anterior horn disclose the same pathological character.

The astrocytes appear slightly degenerated, especially in the area of the diencephalon, thalamus, corpus striatum, and infundibulum. The oligodendroglia shows here and there slight swelling especially in the white substance, whereas, the microglia appears grossly normal.

The blood vessels disclose occasionally slight swelling of the endothelial lining cells and occasional slightly degenerative changes of these elements.

Cat No. 4—Lab. 18. Weight 2,900 grams.

Animal was injected for the first time on December 11, 1931, with 100 mg. of indol. Following injection animal seemed restless and rather weak. Following daily successive doses no marked reactions were elicited. The animal had altogether 107 injections of 100 mg. each in the course of 138 days. Clinically, from a neurological standpoint, the animal appeared normal. Animal was killed on May 1, 1932, by air injection in the femoral vein. With the Nissl stain the nerve cells show slight degenerative changes which are somewhat more diffuse than analogous degenerative changes detectable in normal animals. The lesions consist in the already mentioned chromatolysis, that is, granular disintegration of the Nissl bodies, diffusion of the chromatin substance, homogenization of the nucleus, and occasionally increased satellitosis. The cell body when involved is slightly swollen and the elements appear in a condition of moderate acute swelling. The process of vacuolization when present is especially appreciable around the nucleus. This phenomenon seems to be especially present in the small cells of the outer layers and more so in the cells of the second and third layers normally having a more roundish aspect. In the frontal and motor regions the lesion seems slightly more pronounced. There is besides a gradual fading out of a certain number of nerve cells, the disappearance of which results in the formation of small acellular areas (Fig. 4).

Altogether the involvement of the nerve cells though evident is only slightly more pronounced than the moderate amount of pathology that we do find in the normal brain.

The changes of the astrocytes are not very pronounced though here and there degenerative elements undergoing swelling and clasmatodendrosis are found in the cortex, in the subcortical structure, as well as in the brain stem and cerebellum. Practically no changes are detectable in the oligodendroglia and microglia.

Histological study of the liver reveals slight fatty degenerative changes surrounding the central venules of the lobule. Better preserved cells but containing fat substance are also seen at a greater distance from the central portion of the lobule.

Cat No. 6—Lab. 10. Weight 3.6 kg.

January 6, 1931: Animal was given first dose of 100 mg. of indol which he received daily and which was increased to 150 mg. on January 9. Up to April 11 the animal has had practically a daily injection of 150 mgs. The animal most of the time has been quiet and inactive.

Some of the protocols read as follows:

March 19, 1931: For the past six weeks the animal has been very unfriendly resenting any attention.

April 3, 1931: Animal has eaten nothing during the past 24 hours. Lies on side with slightly increased respiration. No injections were given for two days.

April 6, 1931: Animal was apparently recovered and was again injected with 150 mg. of indol.

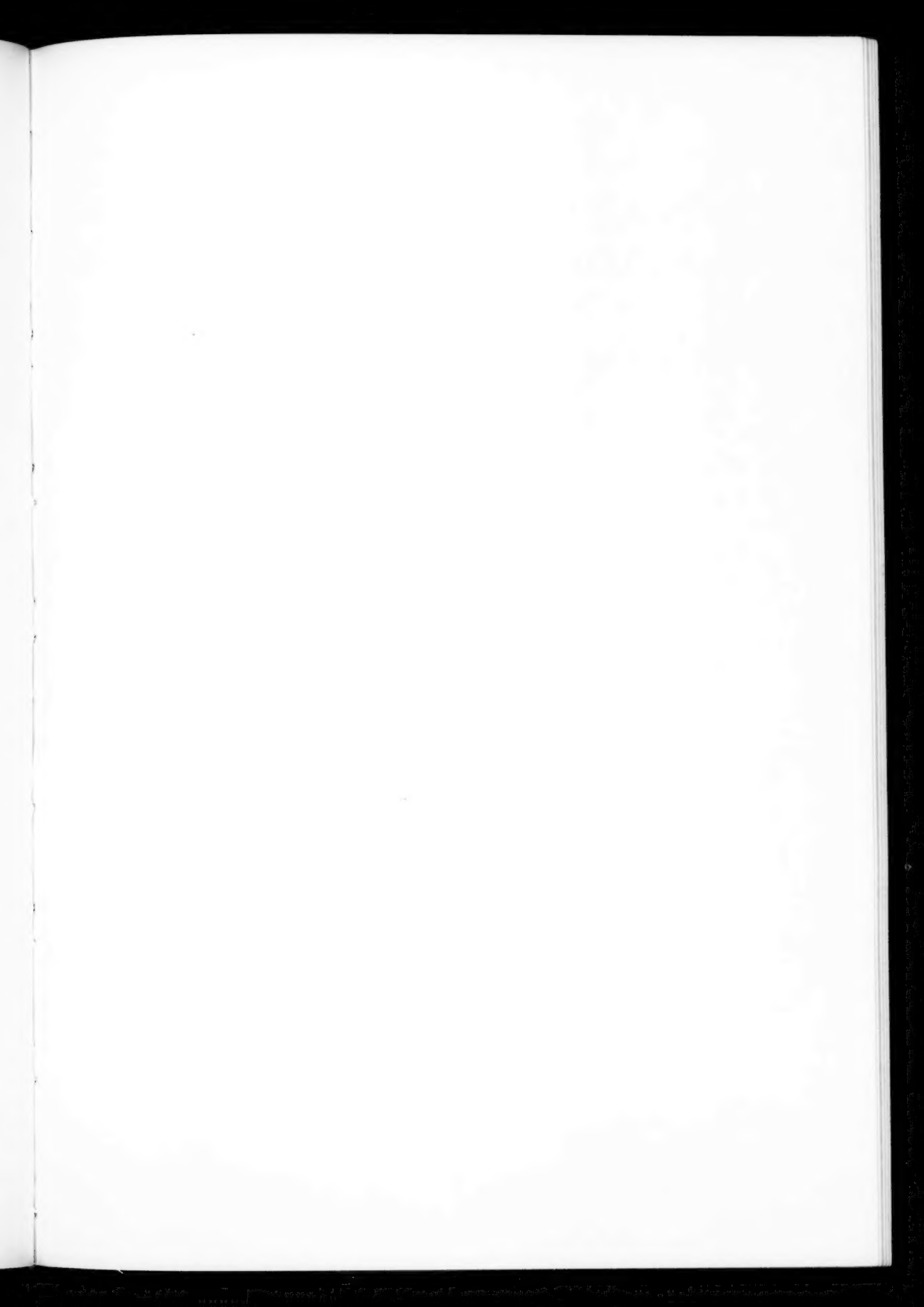
April 8, 1931: Weight of the animal has fallen to 2.16 kg.

April 9, 1931: Animal was weak and disclosed no appetite at all. Animal not injected on this day nor on the following day as it appeared quite weak.

April 11, 1931: Animal died.

Altogether this animal had three injections of 100 mg. each and 73 injections of 150 mg. each in the course of 95 days.

Histological Study: With the Nissl stain the nerve cells show diffuse degenerative changes which can be classified under the heading of the severe type of degeneration of Nissl consisting in the gradual disintegration of the Nissl bodies and the appearance of small ring-like formations in the cytoplasm. Some of the nuclei, however, appear swollen and gradually disintegrate without passing apparently through a stage of pyknosis. Numerous other nerve cells appear swollen and gradually disintegrating, the pro-



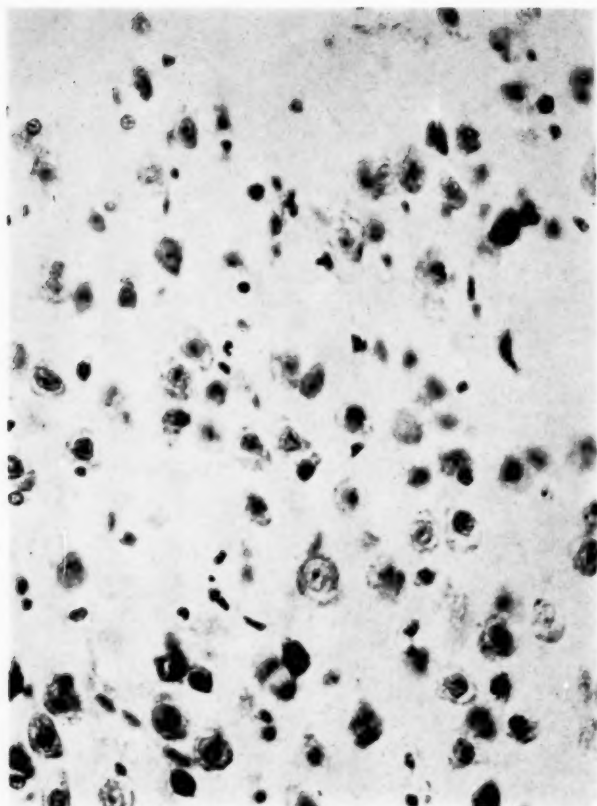


Fig. 5. Pronounced liquefaction of nerve cells represented by vacuolization and gradual disintegration of the element. Nissl stain for nerve cells

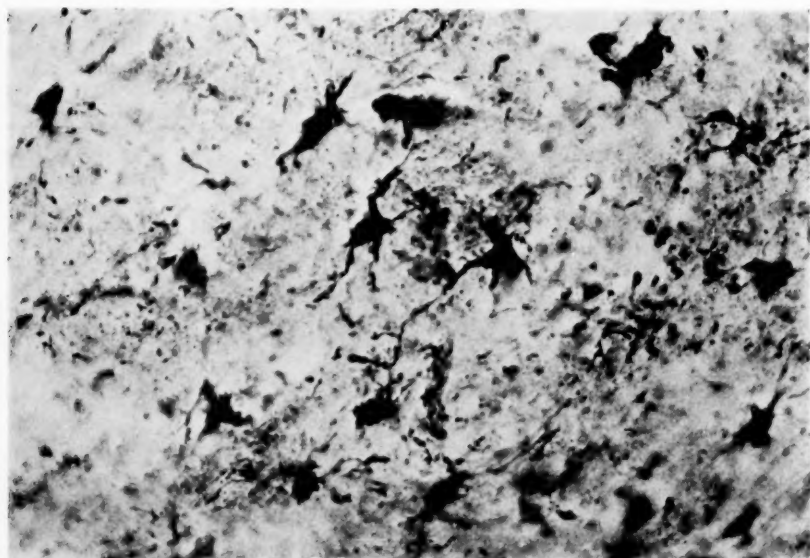


Fig. 6. Severe degenerative changes of astrocytes. Cajal gold sublimate method

cesses becoming irregular and broken and the whole element gradually fading out through a gradual process of liquefaction (*Verflüssigung*) (Fig. 5). It seems as though the process of vacuolization originates around the nucleus, gradually spreading into the cytoplasm and leading to the complete disintegration of the element. Neuronophagia is evident and degenerative changes are detectable in the nuclei of the glia elements performing such a function. There is no question here that the changes are pronounced and diffuse and involve not only the cortex but the basal ganglia, the infundibulum, the brain stem, the cerebellum, the medulla oblongata, and the spinal cord. Here also the fact might be mentioned that the lesions are more pronounced in the outer layers of the cortex.

The astrocytes show definite degenerative changes consisting in swelling and granular disintegration of the cytoplasm, swelling and tortuosity of the processes (Fig. 6). The processes at times have a terminal swelling or may disclose swelling intercalated with a normal structure, occasionally giving the impression of a moniliform or rosary bead appearance. Clasmotodendrosis is definitely marked and seems to be more pronounced in the diencephalon, in the globus olfactorius posterior and in the frontal and temporal cortex.

In the cerebellum, where numerous Purkinje elements are seen undergoing not only homogenization but also gradual disintegration leading to the disappearance of the elements, the granular layer shows more definite tendency towards conglutination though as yet not so pronounced as in cases of indol poisoning associated with histamin or KCN. In the cerebellum degenerative changes of the astrocytes are less pronounced and involve the molecular and granular layers.

The oligodendroglia appears slightly swollen but definitely so all over the brain, whereas the microglia elements disclose a slight peculiar atrophic type of reaction consisting in a certain amount of shrinkage of the cell body. The elements appear somewhat smaller, the cytoplasm surrounding the nucleus being practically absent and the nucleus appearing shrunken. No tendency of the microglia to acute swelling nor to transformation into scavenger elements is seen.

The blood vessels disclose only slight degenerative changes of the endothelium. No proliferative changes nor exudative elements are found.

Cat Binky—Lab. 78. Weight 3,600 grams.

Animal received a daily dose of 200 mgs. of indol from February 24 to March 28, 1932. Altogether the animal received 32 injections with a total of 6,400 mg. At the time of its death, March 28, 1932, the animal weighed 2,780 grams.

Histological Study: The main feature is represented by a severe type of degeneration of the nerve cells which are seen undergoing all types of changes from the acute swelling to the complete disintegration. Numerous nerve cells disclose a vacuolar ring surrounding the nucleus which appears swollen and only occasionally shrunken or pyknotic (Fig. 7). It is of interest to note here that only here and there the nucleus discloses deformities in the sense of shrinkage and karyorrhexis. Indol as a whole seems, apparently to have a predilection for the cytoplasm rather than the nuclear portion of the nerve cell. The Nissl bodies undergo gradual disintegration and the cytoplasm appears poorly stained and more or less substituted by large vacuoles which, as already said, begin surrounding the nucleus. In a few areas, however, the nerve cells appear altogether shrunken, the cytoplasm being quite pale while the nucleus is deformed and deeply stained, a condition recalling more the so-called ischemic type of lesion of the nerve cells.

The degenerative process involving the nerve cells is a quite pronounced one and quite diffuse but not so severe as in the cases where indol poisoning is associated with histamin.

In the white matter, but especially at the boundary between gray and white matter, there exists surrounding some of the blood vessels and more so surrounding the veins a proliferation of glia elements most of which appear to be oligodendroglia and microglia. The condition recalls to a very moderate degree what has been described in some special forms of encephalopathy, as for instance, measles and vaccine encephalopathy, in which this perivascular proliferation is the dominant characteristic of the pathological process.

The Cajal gold sublimate method for neuroglia reveals diffuse degenerative changes of the astrocytes, not very different from the ones described in the previous animal, though the intensity of the degenerative changes is slightly more pronounced.

The oligodendroglia discloses a slight condition of acute swelling which is particularly observable in the white matter. The degree of the swelling is a moderate one. Here and there slight progressive changes of the element in the sense of slight hypertrophy of the cytoplasm is seen.

The microglia cells appear grossly normal though here and there the small cell bodies are somewhat shrunken and deeply stained.

The lining endothelium of the intima in the cortical blood vessels discloses a certain amount of hypertrophic changes consisting mainly in a certain increase in size of the nucleus which occasionally is accompanied by some swelling of the surrounding cytoplasm.

The liver discloses a marked fatty degeneration (Fig. 8) which in some

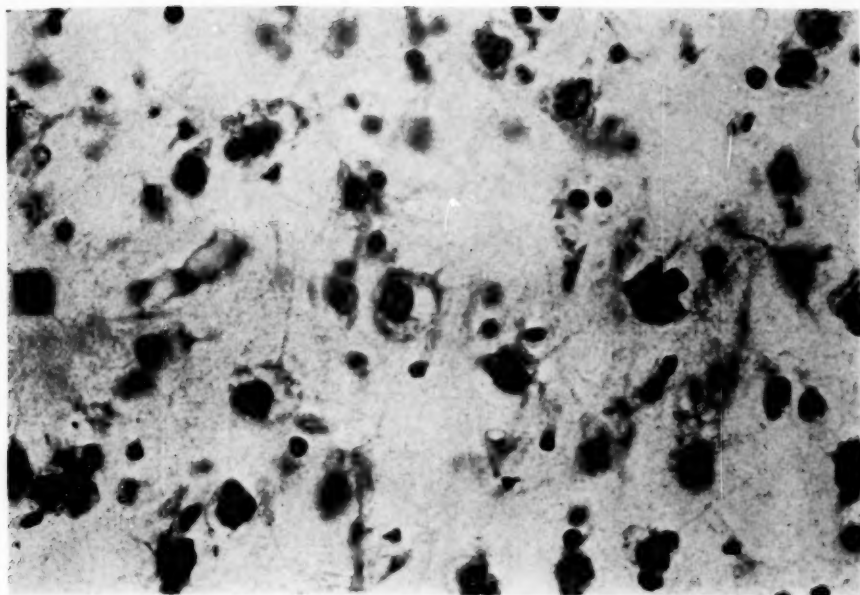


Fig. 7. Marked liquefaction of cytoplasm of nerve cells with better preservation of the nuclei. Nissl stain for nerve cells

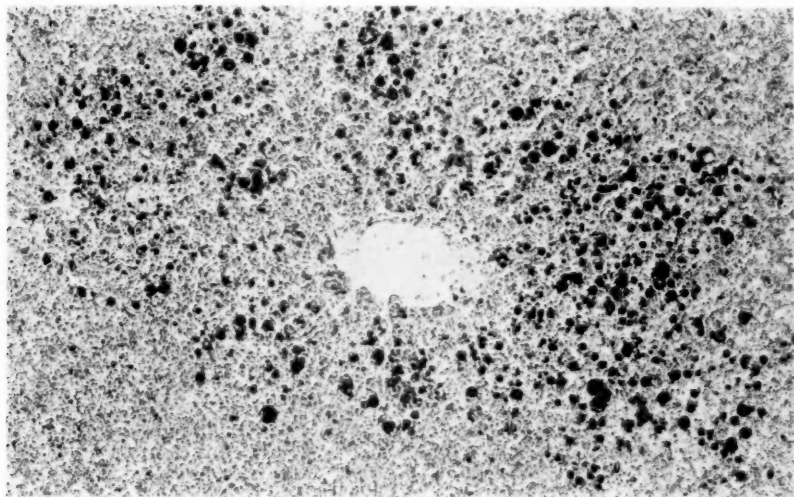


Fig. 8. Fatty degeneration centrally located. Fettepenceau stain for fat products of disintegration

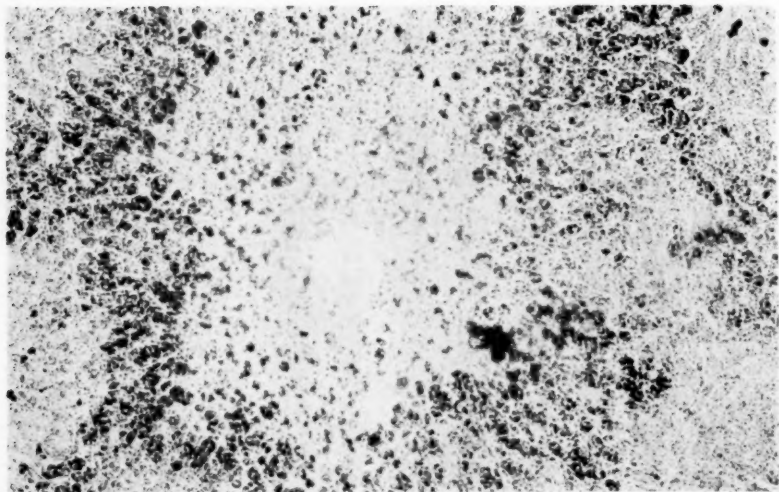


Fig. 9. More advanced stage of fatty degeneration leading to marked disintegration of the central portion of the lobule. Fettepenceau stain for fat products of disintegration



Fig. 10. Small intestine disclosing hyperplasia of lymphoid tissue, atrophy of the mucosa and hypersecretion of mucous. H & E stain

areas is quite central in distribution. In more advanced areas the central portion of the lobule is considerably degenerated, whereas the fat products of degeneration are seen in the cellular elements at the periphery of the lobule (Fig. 9).

The small intestine discloses a considerable amount of lymphoid hypertrophy and invasion of the lymphoid elements in most of the villi. The epithelial covering of the villi is more or less degenerated and signs of mucoid hypersecretion are noticeable (Fig. 10). The large intestine discloses also lymphoid hypertrophy and invasion of lymphoid tissue from the submucosa into the mucosa. Marked hypersecretion of mucous (Fig. 11) is evident.

Cat No. 5—Weight 2,950 grams.

Animal was injected with daily doses of 50 mg. of indol starting on December 15, 1930. Animal has received 114 daily injections of 50 mg. of indol between December 15 and May 27. Animal then had 160 injections of 100 mg. each from May 28, 1931 to February 10, 1932. During all this time the animal did not show any appreciable clinical manifestations. The animal is at the present time being used for an experiment in which histamin has been associated with indol.

B. EXPERIMENTAL HISTAMIN POISONING

The histamin used in our experiments is the one prepared by Hoffman La Roche, in ampoules of 1 mg. of histamin in 1 c.c. of distilled water.

Cat C—Lab. 20. Weight 3.200 kg.

Injection on February 5 of 5 mg. of histamin. Animal was very quiet afterwards. No immediate reaction. One hour and fifteen minutes later three more mg. were administered by subcutaneous injection. Some contraction of the pupils appeared but no other immediate effect.

February 6, 1931: 7.5 mg. of histamin was given in one dose. Animal vomited in ten minutes and again 20 minutes later. Immediately after injection there was marked salivation and increased respiration which lasted for 35 minutes. Thirty minutes after the injection animal showed slight tremor of the head and body muscles. During the next hour following the injection animal was very quiet, exhibiting what might be termed slight narcosis from which it could be easily aroused. The foot pads were very dry.

February 10, 1931: Animal received 8 mg. in one dose and disclosed only a slight narcosis.

May 1, 1931: Animal again injected with 8 mg. Animal very quiet after injection and had loose stools immediately after.

May 6, 1931: Animal received 8 mg. of histamin. Bowel movement immediately followed and vomiting appeared within ten minutes.

May 7, 1931: Animal received 10 mg. of histamin and vomiting appeared in 10 minutes.

May 13, 1931: Animal received 12 mg. of the drug. There was immediate salivation, bowel movement in 20 minutes.

May 18, 1931: Animal had an intravenous injection of 6 mg. of histamin following which it died.

Histological Study: Nissl stain shows that a certain number of cells are undergoing a process of chromatolysis which is quite definite but not very intense. A comparison with the normal cells of the motor cortex discloses the quality of the change. In the nucleus there is a process of granular disintegration of the chromatin substance which is evident especially in the frontal area and in the large pyramidal cells of the motor cortex. There is, however, no severe type of lesion nor liquefaction of the cytoplasm. Perhaps in the outer layers a few more cells are present than in the normal showing slight annular vacuolization surrounding the nucleus.

The glia tissue appears normal and so are the microglia and oligodendroglia elements. No appreciable changes of the endothelium of the blood vessels.

Altogether, there seems to be a slight increase over the number of cells which in a normal cat show degenerative changes, with the addition that following histamin poisoning the lesions seem to appear more marked in the nucleus.

Cat A—Lab. 70. Weight 2.3 kg.

Animal was given first dose of one mg. of histamin subcutaneously on December 1. About three minutes after injection cat appeared slightly stuporous with slight muscular weakness, marked dilatation of the pupils and rapid beat of the heart. In five minutes there appeared a fibrillary twitching of the left front foot. The twitching was of short duration disappearing in a few minutes, after which the animal behaved in a normal manner.

December 2, 1930: 1.5 mg. of histamin was administered and the twitching of the hind leg developed in 10 minutes lasting about two or three minutes. Animal appeared drowsy during the afternoon.

December 3, 1930: 1½ mg. of histamin was injected and in about 20 minutes the animal became very quiet and appeared drowsy. There was a slight increase in respiration but no twitching.

December 4, 1930: The dose of histamin was increased to 2 mg. and a

slight twitching of the right hind leg occurred, which was of very short duration.

December 5, 1930: Dose was increased to 3 mg. There was slight twitching of the hind leg in 10 minutes, which was of very short duration. Nothing else except slight increase in respiration.

December 8, 1930: From this day on no marked reactions were present.

December 12, 1930: Slight vomiting appeared and from then on the animal received daily doses of 3 mg. of histamin up to February 10, 1932. Altogether this animal received 324 injections of 3 mg. each of histamin and the only appreciable clinical symptom was movement of the bowels immediately following injection and generally more quiet behavior than the normal animal.

February 10, 1931: Dose was increased to 5 mg. daily. Altogether then the animal has received 324 injections of histamin with no appreciable clinical changes and also 30 injections of 5 mg. each. Animal was killed March 9, 1931.

During the last month following injection of 5 mg. of histamin the movement of the bowels following injection was a constant feature and the heavy breathing always followed the administration of the drug. In addition there was a marked congestion of the ears, nose and mouth. On two occasions there has been vomiting following the injection.

Histological Study: The Nissl stain reveals the existence of degenerative changes which, however, are very slight and consist in a moderate amount of chromatolysis. A few nerve cells show beginning signs of vacuolization, the vacuoles appearing first surrounding the nuclear region. Only occasionally cells are seen having undergone a complete process of liquefaction. The nuclei of the nerve cells seem to undergo also a process of bleaching and are a great deal paler than usual. The glia nuclei as detected by the Nissl stain do not show appreciable changes contrasting with the pyknosis found in indol poisoning. The blood vessel walls do not reveal appreciable changes.

With appropriate stain for oligodendroglia and microglia both these elements appear practically intact. There is a certain amount, however, of acute swelling of the oligodendroglia but this pathological process is very moderate and not extremely diffuse. It is also true that here and there a few microglia cells are gradually fading out from the section, but altogether the majority of the elements appear well preserved.

The gold sublimate method of Cajal for astrocytes shows very slight changes consisting of a certain amount of swelling of the cell body and a regular swelling of the processes with an occasional rosary bead appear-

ance. The changes are, however, very moderate and are found only in small areas corresponding to the major involvement of the nerve cells. A large number of astrocytes appear normal, however, in both gray and white matter. Slight predominance of the lesion can be located in the frontal area and hypothalamus.

Histological study of the lung reveals no appreciable changes. The kidneys appear normal. In the spleen there is slight hypertrophy of the lymphoid nodules and certain proliferation of the germinal centers. In contrast the liver shows a marked fatty infiltration, particularly pronounced at the periphery of the lobules.

Cat Arabella—Lab. 76. Weight 2,360 grams.

Animal was injected with increasing doses of histamin from February 25 up to March 24, 1932. The histamin which was used in this experiment consisted of histamin in powder form dissolved in our laboratory in a proportionate amount of water and then sterilized. From this solution ampoules were prepared, some in the proportion of one mg. of histamin to 1 c.c. of water, and others in the proportion of 10 mg. of histamin to 2 c.c. of water.

The animal received altogether 27 injections of histamin, a total of 705 mg. During the last 11 days the animal received four doses of 40 mg. each and seven doses of 50 mg. each.

Histological Study: There are diffuse lesions of the nerve cells but their intensity is rather moderate and not comparable with the more severe lesions obtained with maximum doses of indol. The lesions consist in general of a process of chromatolysis in which the chromatin bodies, especially of the large cells, undergo a process of pulverization and gradual disappearance, the cytoplasm resulting appearing quite homogeneous though fundamentally granular (Fig. 12). In the smaller elements the chromatolysis is more advanced and the process of vacuolization may be seen and consisting in a ring-like formation surrounding the nucleus. The vacuoles in some elements spread all over the cytoplasm and gradually lead to the liquefaction of the cell body. The process of severe liquefaction is not so commonly found, whereas, more frequently a partial vacuolization is encountered characterized by the existence of one or more vacuoles generally located at one of the poles of the nerve cells. The nucleus appears homogeneously stained, the chromatin being gradually broken down and disappearing. The nucleolus is quite resistant to the process of disintegration. There is, however, no swelling of the nucleus but rather a tendency towards a slight shrinkage of the structure. The involvement of the glia nuclei as detected

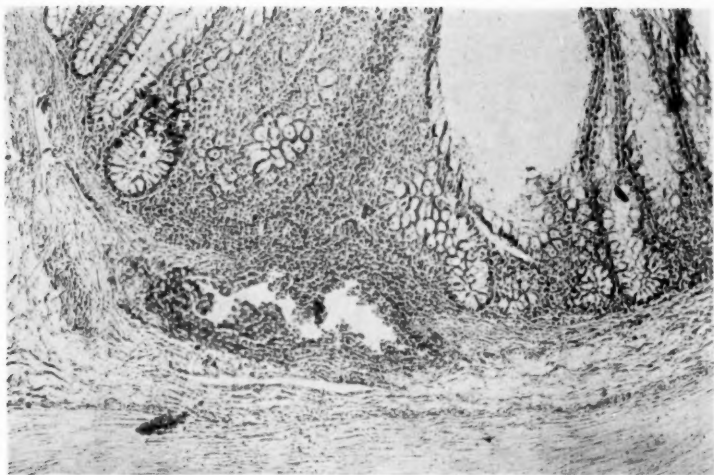


Fig. 11. Large intestines showing hyperplasia of lymphoid tissue, breaking from the submucosa into the mucosa. Marked hypersecretion of mucous. H & E stain

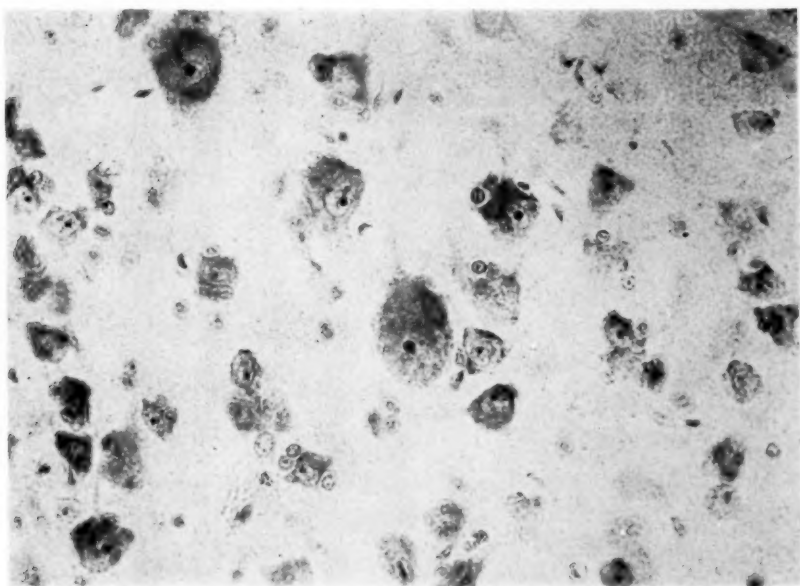


Fig. 12. Diffuse chromatolysis of the Nissl bodies contrasting with absence of vacuolization. Nissl stain for nerve cells

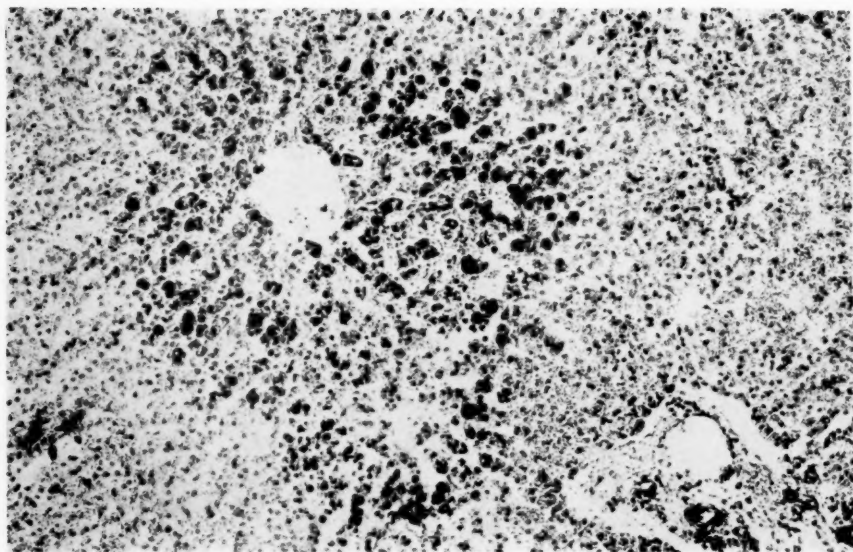


Fig. 13. Fatty degeneration of the liver spreading from the central portion to the periphery of the lobule. Fettepenceau for fat products of disintegration

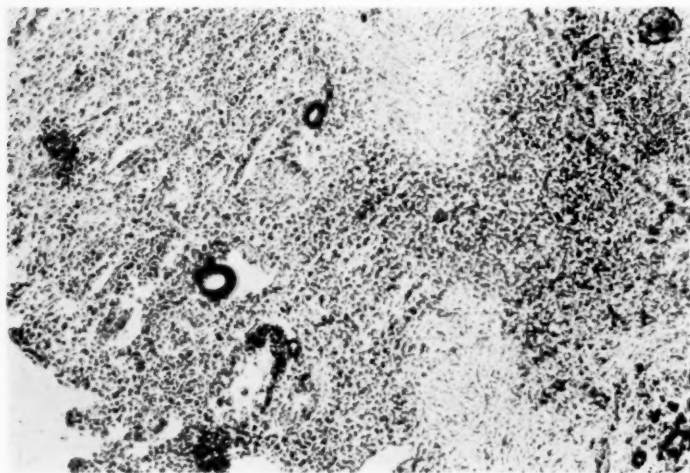


Fig. 14a. Large intestines disclosing hyperplasia of lymphoid tissue and atrophy of the mucosa. H & E stain



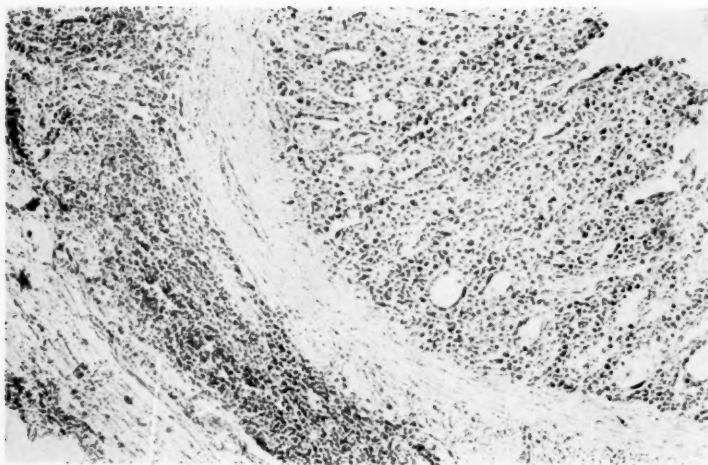


Fig. 14b. Small intestines showing the same hypertrophy of the lymphoid tissue and atrophy of the mucosa. H & E stain

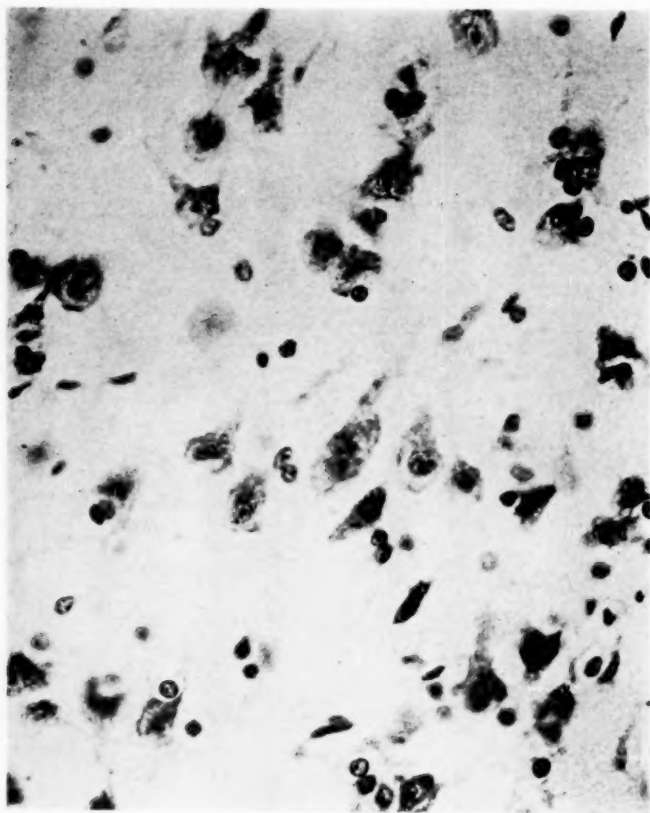


Fig. 15. Severe type of degeneration of the nerve cells consisting in liquefaction and gradual disintegration of the elements. Nissl stain for nerve cells

by the Nissl method does not seem very pronounced. As a result of the destruction of some of the nerve cells the lamination is slightly disturbed and acellular areas are found here and there.

The astrocytes show very slight degenerative changes in the basal ganglia and fronto-temporal cortex. The Ammon's horn discloses, however, normal elements. Micro and oligodendroglia appear normal with the exception of some swelling of the oligodendroglia.

The liver shows a considerable amount of fatty infiltration concentrically located around the central portion of the lobule (Fig. 13). Small fat granules are also seen in the remaining cells.

The large intestine shows increase of the lymphoid tissue in the mucosa and submucosa (Fig. 14a). In the villi of the mucosa fatty degeneration is found quite diffusely and large vacuoles between the villi are detectable. In some of them the lymphoid tissue plaques of the submucosa break into the mucosa through the muscularis mucosa. The same changes are detectable in the small intestine (Fig. 14b) where the submucosa appears slightly hypertrophic and discloses at the same time a certain amount of fat infiltration.

C. EXPERIMENTAL POISONING WITH INDOL AND HISTAMIN COMBINED

Cat E—Lab. 22. Weight 3 kg.

April 8, 1931: Animal injected with 100 mg. of indol followed by another injection of 3 mg. of histamin. The animal received a total of 26 injections of both drugs in the course of 40 days.

May 19, 1931: Animal died at 10 a. m. Weight 2.7 kg.

Histological Study: There are definite changes of the nerve cells consisting essentially in the so-called severe type of lesion of Nissl. The lesion is represented by a diffuse chromatolysis of the cells which appear more or less swollen and the nuclei of which are considerably pyknotic. In the cytoplasm the Nissl bodies are transformed into small ring-like granules extending also in some of the processes which appear swollen and fragmented. Elements are seen in all stages of degeneration from an early stage of breaking down of the Nissl bodies to a stage of complete fading of the cell. A few elements possess large clear nuclei deprived of chromatin substance. In this case the nerve cell has the tendency to gradually fade out from the section. Conversely, in the elements where the nucleus is more or less pyknotic a more or less extensive vacuolization is present (Fig. 15) and at times invading the whole cellular body and resulting in complete liquefaction.

The glia nuclei with the thionin stain appear considerably shrunken and most of them undergoing a process of karyorrhexis. A few glia elements are seen with staining methods undergoing ameboid changes. The cellular lesions are more pronounced in the frontal area, the hypothalamus, infundibular region, corpus geniculatum laterale and cerebellum. In the cerebellum the Purkinje cells show severe degenerative changes from a simple process of homogenization to a process of vacuolization and complete disintegration. There is also a definite process of conglutination of the cells of the granular layer.

In the brain stem and medulla oblongata numerous nerve cells are found in the formatio reticulata and in the various nuclei of the cranial nerves disclosing the same fundamental changes of the severe type. In the spinal cord numerous cells of the anterior horn are severely involved and disclose a more or less complete process of disintegration.

The astrocytes show diffuse degenerative changes distributed all over the various cortical territories but more pronounced in the second and third layers. The degenerative changes are very pronounced in the hypothalamus and in the area of the vegetative diencephalic centers. The changes consist in swelling, vacuolization of the cytoplasm and deformity and swelling of the processes and a more or less advanced clasmatodendrosis (Fig. 16). Besides degenerative changes progressive changes (hypertrophy and hyperplasia) of the astrocytes are found in the hypothalamic region. The oligodendroglia shows diffuse acute swelling especially of the white matter. In addition to the acute swelling there are a certain number of elements having undergone a slight process of hypertrophy and which disclose a beginning vacuolization of the cytoplasm.

The microglia shows a certain number of elements which appear normal but others disclose degenerative changes represented by homogenization of the cytoplasm and of the nucleus, swelling and deformity of the cell body and of the processes. A few elements are found with a rather shrunken appearance pointing to a possible atrophic reaction.

With the Spielmeyer method patches of demyelination are found (Fig. 17) in which at higher power myelin remnants are encountered under the form of myelin balls or myelin sheaths with ball-like endings. Swollen myelin sheaths are also found in an early stage of fragmentation.

The blood vessels show a certain amount of swelling of the endothelium and degenerative changes of the cells but no progressive changes.

Histological study of the liver reveals a severe fatty degeneration of the lobules, more pronounced in their central portion.

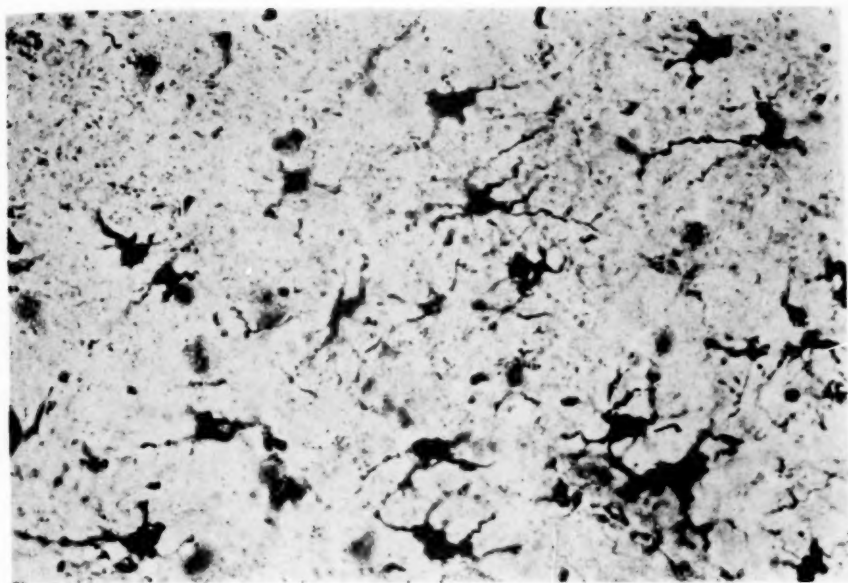


Fig. 16. Severe degenerative changes of astrocytes (note swelling and breaking down of the processes). Cajal gold sublimate method

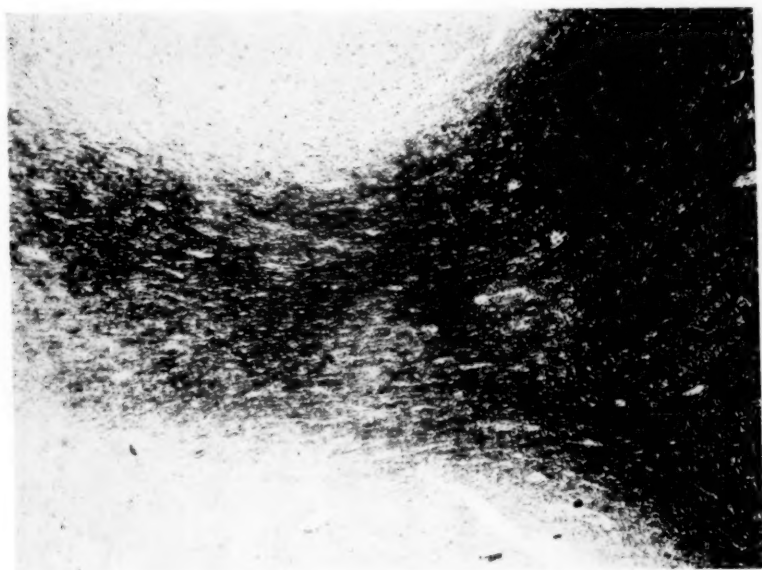


Fig. 17. Patches of demyelination especially pronounced in the subcortical areas. Spielmeyer stain for myelin sheaths

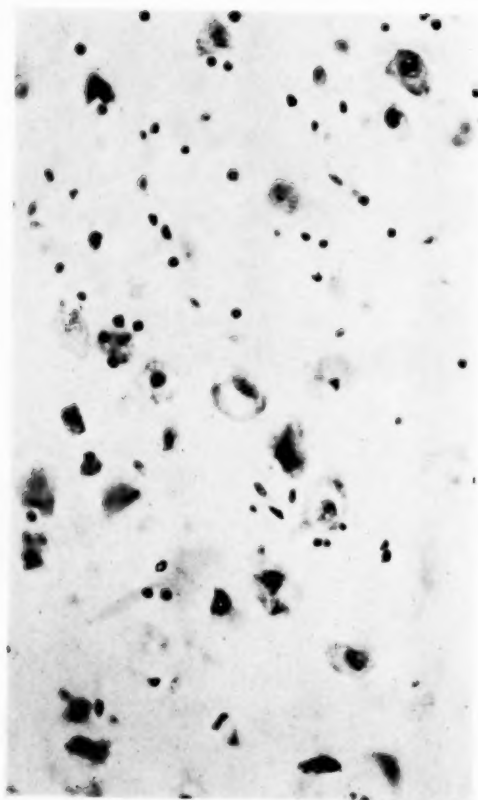


Fig. 18. Severe type of lesion of the nerve cells with marked pyknosis of the nuclei.
Nissl stain for nerve cells

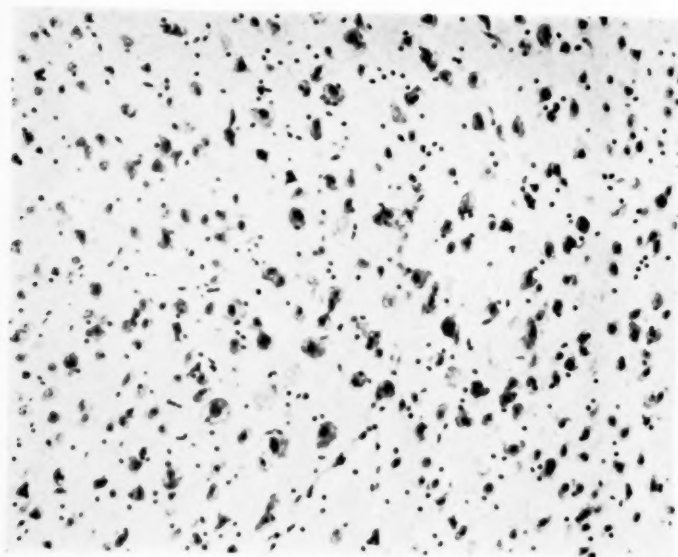


Fig. 19. Diffuse bleaching of the cytoplasm of nerve cells contrasting with pyknosis of the nuclei (ischemic lesion of the nerve cells). Nissl stain for nerve cells

Cat D—Lab. 5. Weight 3,000 grams.

March 2, 1931: Starting with this day animal was injected daily with 150 mg. of indol followed by 3 mg. of histamin. Altogether the animal received 9 injections of the two drugs.

A few of the protocols read as follows:

March 11, 1931: Animal was very quiet and inactive.

March 13, 1931: Animal lies on side, mildly narcotic, refuses food and appears quite toxic. Indican in the urine.

March 14, 1931: Animal died.

Histological Study: Nissl stain reveals the existence of very severe degenerative changes of the nerve cells scattered all over the cortex, the sub-cortical structures, the brain stem, medulla, cerebellum and spinal cord. The lesions are more pronounced in the frontal and motor areas, in the caudate nucleus, in the hypothalamus, and infundibular region.

The lesions consist essentially in the so-called severe type of disease of the nerve cells and are mostly represented by a severe process of vacuolization which begins around the nucleus, invades the cytoplasm and leads to a complete liquefaction of the cellular element (Fig. 18). The nucleus undergoes general regressive changes and appears shrunken and often deeply stained. All grades of transition are found from the early vacuolization to the complete liquefaction of the cells. The cellular processes are occasionally visible and they appear swollen and fragmented. In the cells of the external layers, which have a more roundish aspect, the liquefaction is visible surrounding the nuclei and the vacuolization seems to have replaced entirely the cellular bodies. In some areas nerve cells are found the cytoplasm of which is homogeneous, the nucleus shrunken and the whole element reduced in size, an aspect recalling somewhat the so-called ischemic type of lesions as described by Spielmeyer (Fig. 19). Transitory stages between such changes and the one of liquefaction are a common occurrence. The neuroglia nuclei surrounding the degenerated cells are for the great majority pyknotic and undergoing a process of karyorrhexis.

In the corpus striatum the changes of the nerve cells are more severe in the caudate nucleus while the claustrum discloses a considerable number of severely degenerated elements. In the infundibular region the nerve cells are severely damaged in the area in which the vegetative centers are located and among these latter the nuclei periventricularis and supraopticus seem considerably involved. In the lobus olfactorius posterior the cellular damage seems also very pronounced. In the cerebellum the majority of the Purkinje elements are undergoing severe degenerative changes represented

by vacuolization and a certain shrinkage of some of the elements which lose their previous normal orientation assuming one of a parallel course to the granular layer (Fig. 20). In some areas the Purkinje cells are entirely invaded and almost substituted by elements of the granular layer (Fig. 21).

The granular layer discloses distinct conglutination of the small cells, which conglutination in some areas is very pronounced, and represented by fusion of granules (Fig. 22) undergoing degenerative changes.

In the mesencephalon and in the metencephalon the *formatio reticulata* appears severely damaged. In the medulla oblongata and in the spinal cord the same severe degenerative changes are found which appear especially pronounced in the motor cells of the anterior horn. Here the cells show the same fundamental changes as described in the brain tissue.

The astrocytes with the Cajal gold sublimate method reveal diffuse degenerative changes leading to deformity of the cell body, deformity of the processes and final fragmentation of these (Fig. 23). Before fragmenting the processes may undergo deformity in the sense of uniform swelling or interpolated swelling which gives to the processes a moniliform or rosary bead appearance. Some of the astrocytes are undergoing a process of gradual disintegration. The changes of the astrocytes are especially pronounced in those areas where the changes of the nerve cells are very severe. They are, therefore, particularly pronounced in the frontal area and in the infundibular region and in the second and third layers of the cortex. In the molecular layer we find that some of the astrocytes seem to undergo progressive changes leading to a process of gliosis especially pronounced in the subpial area.

The oligodendroglia elements show a diffuse acute swelling. Only occasionally hypertrophic elements are found in which hypertrophic changes have taken place followed by slight vacuolization.

The microglia elements show a combination of degenerative and proliferative changes. The degenerative changes consist generally in the homogenization of the cytoplasm and nucleus, a slight degree of swelling and a more or less advanced process of disintegration of the whole element preceded or not by a process of clasmotodendrosis. There are, however, especially in the white matter, signs of progressive changes of the microglia represented by an increase in the number of the elements which seem to have a tendency to form a sort of perivascular proliferation suggestive of a somewhat analogous process which we do have in other toxic encephalopathies. In the white substance definite areas of demyelination are found. Demyelination, however, is not perivascular in nature but seems to be somewhat more diffuse though somewhat lighter areas are found surrounding the blood

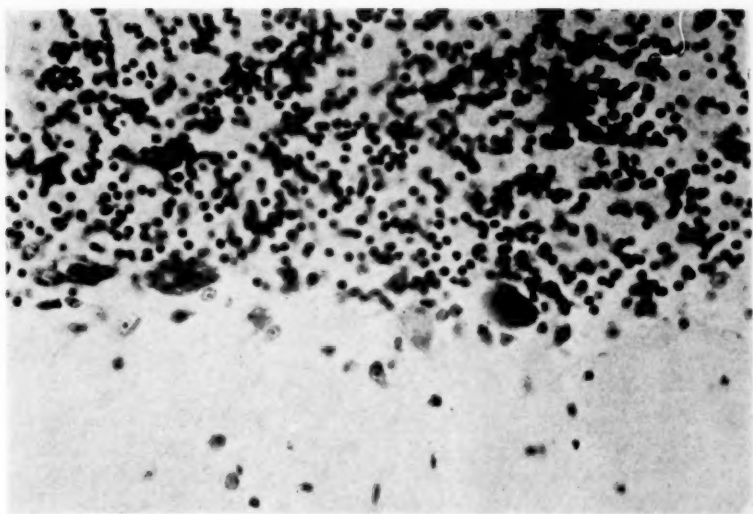


Fig. 20. Severe degeneration of nerve cells of the Purkinje layer. Nissl stain for nerve cells

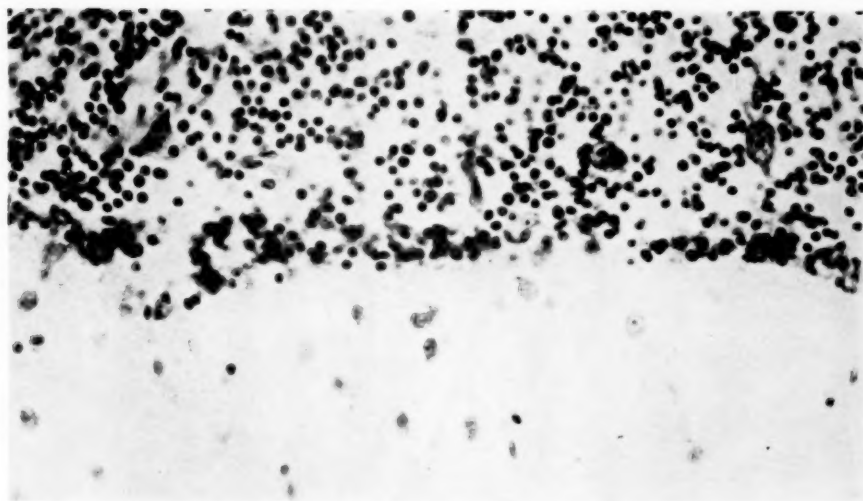
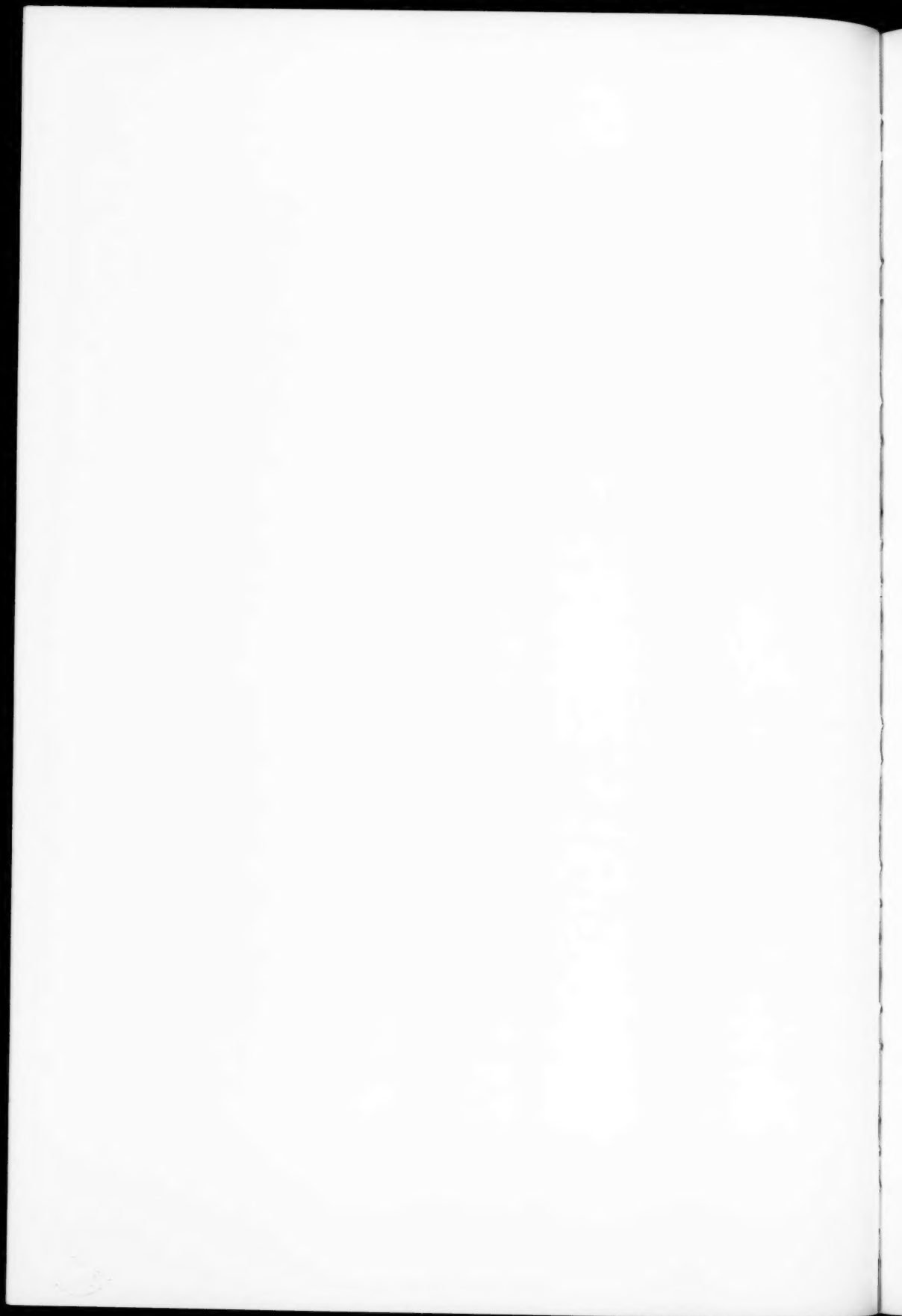


Fig. 21. Severe destruction of Purkinje elements and substitution by elements of the granular layer. Nissl stain for nerve cells



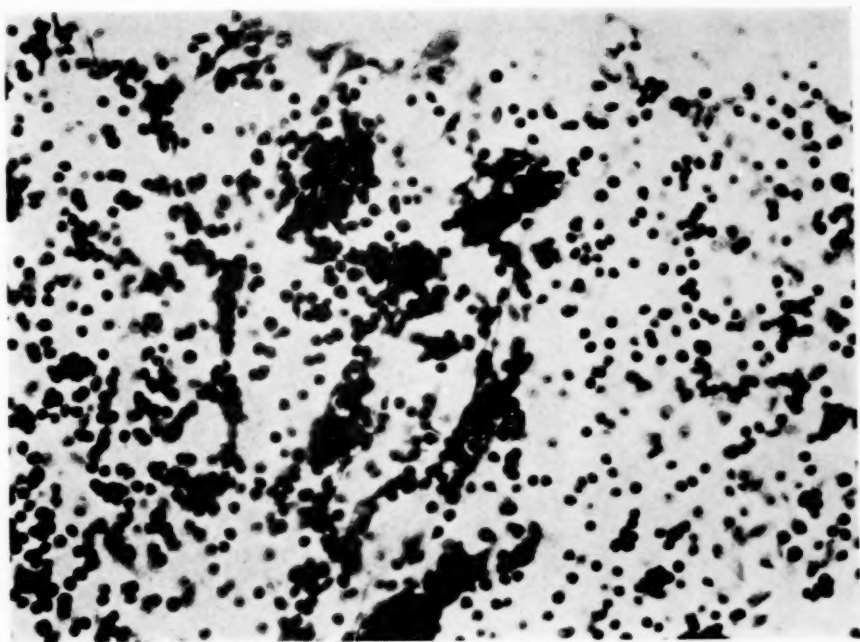


Fig. 22. Conglutination of the cellular elements of the granular layer. Nissl stain for nerve cells

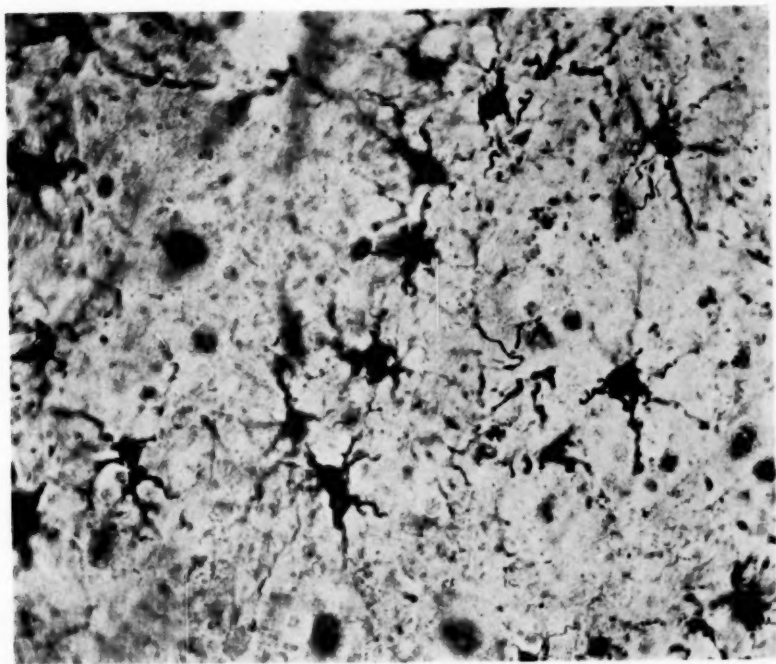


Fig. 23. Severe degenerative process of astrocytes. Cajal gold sublimate method

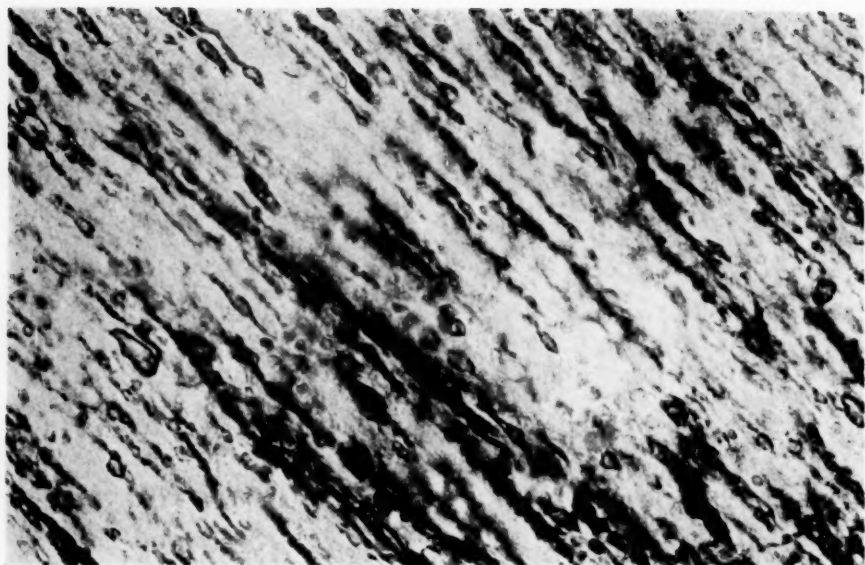


Fig. 24. Details of degenerative changes of the myelin sheaths (Note fragmentation and myelin ball formation). Spielmeier stain for myelin sheaths

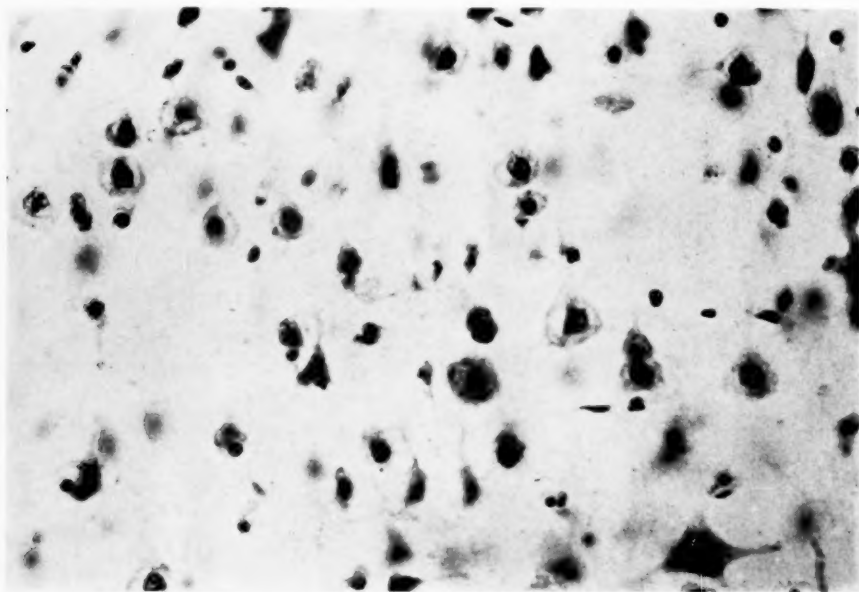


Fig. 25. Severe type of degeneration of nerve cells leading to disintegration and disappearance of the element. Nissl stain for nerve cells

vessels. The process of demyelination is especially definite at the periphery between the gray and white matter. In the more severe demyelinated areas remnants of myelin sheaths are found and other sheaths undergoing all grades of degeneration from the stage of uniform acute swelling to the one of myelin ball formation and granular disintegration (Fig. 24).

The blood vessels, in the surroundings of which such elements are found, show no definite progressive changes.

Cat No. 8—Lab. 19. Weight 2,600 grams.

Animal was first injected on March 19 with 150 mg. of indol followed by another injection of 4 mg. of histamin. From this date to May 8, 1931, animal received 33 injections of 150 mg. each of indol and 16 injections of 4 mg. each of histamin. Immediately following the first injection of indol and histamin the animal had bowel movement, salivation, and was nauseated. Respiration increased. Mild narcosis with constricted pupil. The second injection of histamin was given on March 30, the third on April 2, the fourth on April 6, the fifth on April 8, the sixth on April 13, the seventh on April 15, the eighth on April 16, the ninth on April 17, the 10th on April 29, the 11th on April 30, the 12th, 13th, 14th, 15th and 16th injections on May, 4, 5, 6, 7 and 8 respectively.

Some of the protocols read as follows:

April 2, 1931: Animal slightly narcotic and shows increased respiration. Recovery takes place in about an hour.

April 6, April 16, April 29, 1931, etc., and everytime the histamin was added to the indol, the animal always had loose stools, occasional vomiting, and appeared very quiet.

May 8, 1931: At autopsy the fat shows throughout the body a golden yellow color. Dura of the brain and cord also bile tinged. Lungs edematous but contain air. Cross section of the liver is yellowish.

Histological Study: There are diffuse lesions of the nerve cells scattered all over the cortex and mainly represented by pallor of the elements and shrinkage of the nucleus recalling somewhat the so-called ischemic type of lesion as described by Spielmeyer. Among these cells numerous elements can be located disclosing the acute severe type of degeneration of Nissl represented by granular disintegration of the cytoplasm, deformity of the nucleus, and presence of more or less numerous vacuoles. The severity of the lesion varies according to the areas but is more pronounced in the fronto-parietal region (Fig. 25). The lesions also seem to predilect the temporal cortex, the diencephalic vegetative centers, and the corpus geniculatum laterale.

In the brain stem and medulla oblongata the lesions are also diffuse and seem to involve most of the cells of the formatio reticulata and the cells of the pontine nuclei. They seem to involve more the red nucleus and the substantia nigra. In the cerebellum the lesions involve both the Purkinje elements and the cells of the granular layer. The Purkinje elements besides their homogenization show shrinkage of the element, vacuolization, and eventually disintegration. The small cells of the granular layer undergo a mild process of conglutination consisting in the degenerative changes of the elements and a tendency of several of them to fuse into conglomerations which at times surround and invade the Purkinje elements.

The neuroglia nuclei as detected by staining methods show for the most degenerative changes consisting in shrinkage and karyorrhexis in both cortex and white matter.

With appropriate stain the astrocytes appear diffusely involved, the lesions being mainly represented by the same degenerative changes already described in the previous animal and in which the element appears slightly swollen, the cytoplasm more or less granular, the nucleus deformed and homogenous and the processes either swollen or fragmented. The hypertrophic changes are not so diffuse and they are more evident in the molecular layer of both brain cortex and cerebellum and in the subependymal layers.

The oligodendroglia elements are for the most actually swollen although a few of them are encountered showing hypertrophic changes in association with more or less degenerative features (slight vacuolization of the cytoplasm).

The microglia seem more resistant to the toxic process, only a few elements being found in a condition of acute swelling. A few others seem to be undergoing degenerative changes represented by homogenization and swelling of the cytoplasm and of the processes suggestive of an atrophic reaction.

The blood vessels show the same fundamental type of reaction as described in previous cases and consisting mainly in a slight swelling of the endothelium and some degeneration of the lining cells but with no definite progressive changes.

The liver discloses severe degenerative changes consisting of a marked degree of fatty degeneration which destroys a considerable amount of the parenchymal cells (Fig. 26). The intestines show fundamentally the same changes as described in previous cases.

D. Experimental poisoning with potassium cyanide alone or in association with indol or histamin: In order to investigate the importance of the

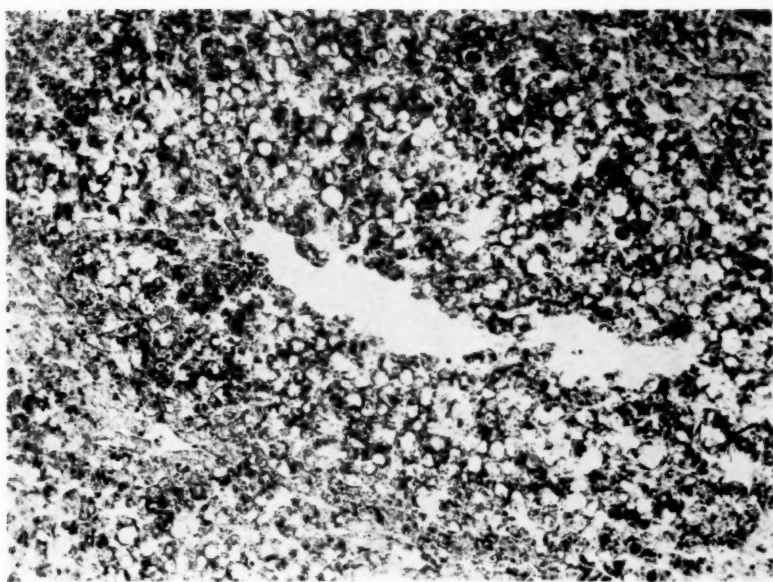


Fig. 26. Severe fatty degeneration of the liver. H & E stain

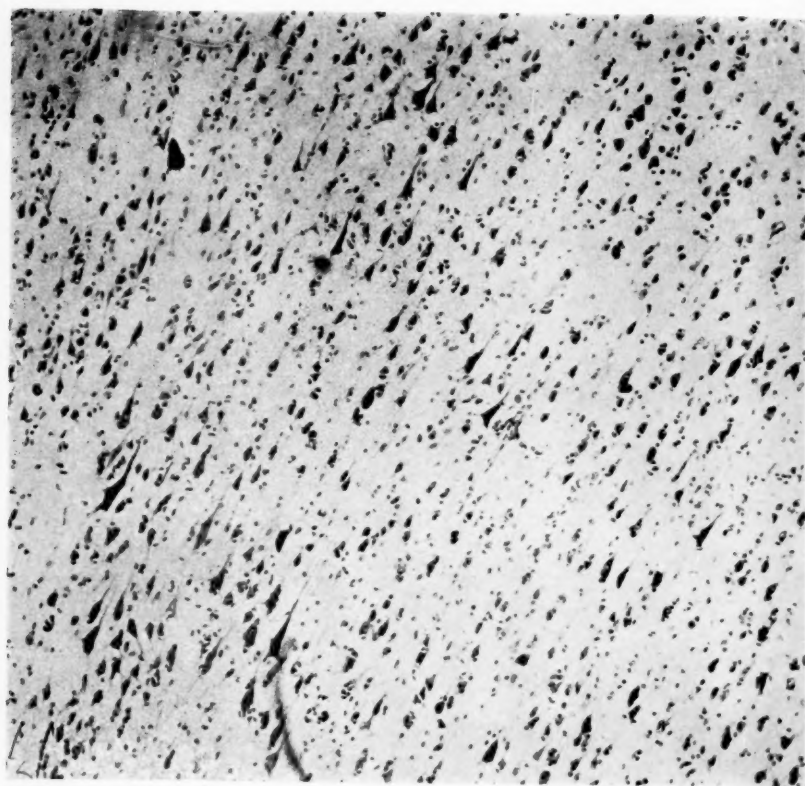


Fig. 27. Shrinkage of the nerve cells. Note shrunken and deeply stained elements.
Nissl stain for nerve cells

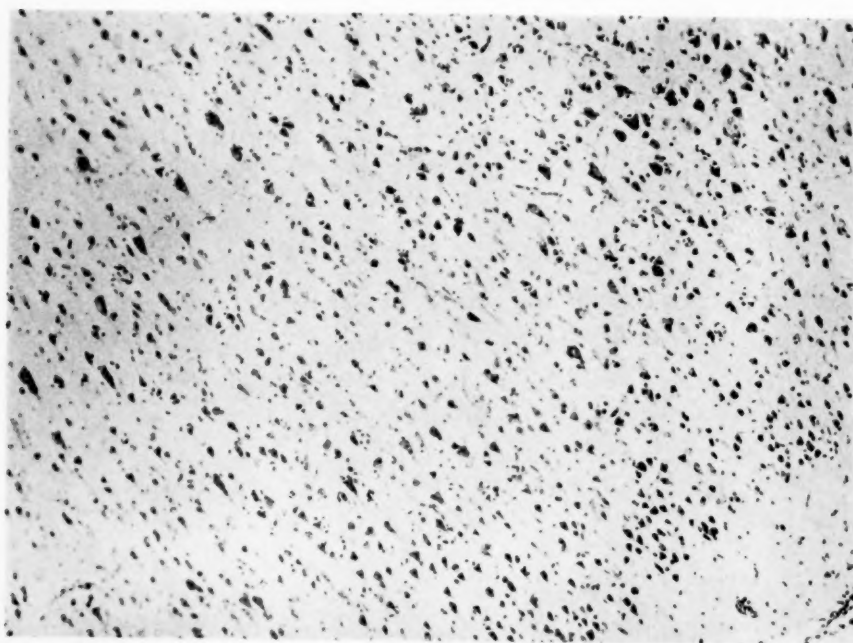


Fig. 28. Normal section of the cortex for comparison with the shrunken appearance
of the nerve cells in Fig. 27. Nissl stain for nerve cells

association of potassium cyanide with indol from the histopathological standpoint, the following experiments were carried, two of which consisted in a control experiment, the animals being injected daily with potassium cyanide alone. Two other animals were injected with potassium cyanide in association with indol and one with potassium cyanide and histamin.

Cat No. 10—Lab. 17. Weight 3 kg.

Animal was injected from March 10 to April 30, 1931, receiving in all 32 injections of potassium cyanide starting with 1 mg. on the first day and gradually increasing by $\frac{1}{2}$ mg., reaching a maximum of 16 mg. on April 24. On April 27 the animal received an injection of 18 mg. Almost immediately defecation, urination, and vomiting followed. Respiration was very fast for over an hour. Some involuntary movements with spasms in extension. Gradually respiration became normal and animal passed into a stage of drowsiness.

April 28, animal injected with 25 mg. The same reaction with recovery. April 29, 30 mg. were injected. Same reaction with recovery. Finally, on April 30, 35 mg. of potassium cyanide were injected with the same reaction and death following in seven hours after injection. Altogether the animal was able to stand approximately 387 mg. distributed over a period of 51 days and given in 32 injections.

At autopsy the blood showed a characteristic cherry color. Lungs seemed congested and the brain shrunken.

Histological Study: Brain cortex showed some cellular changes consisting in shrinkage of the nerve cells. The elements involved appear smaller in size, the Nissl bodies collected together and masking more or less the nuclear structure. This shrinkage of the Nissl bodies is shown by deeper stain of the nerve cells, the contours of which are irregular and the processes of which are occasionally tortuous (Fig. 27). A comparison with a normal cortex (Fig. 28) will better enhance the peculiar shrunken appearance of the nerve cells.

Not all the involved elements, however, appear deeply stained and some, though grossly shrunken, do not present conglutination of the Nissl bodies. As a matter of fact, some of the cellular elements disclose even degenerative changes of the type of chromatolysis but not accompanied by swelling of the cytoplasm.

Here and there there is a more marked evidence of the perineuronal spaces which seems to point to a condition of shrinkage of the cellular unit as a whole. There are, as a matter of fact, no signs of hydropsy of the intercellular substance or of the subcortical structures nor of the choroid plexus

as is the case when an edematous condition is responsible for the dilatation of the perineuronal spaces.

It must be added here that the cellular involvement is not a diffuse one and that numerous elements are seen to be quite normal and that the lamination as a whole is well preserved. Altogether the cortical involvement is not marked and the type of lesion of the nerve cells is of a quite different nature than the one found in indol and histamin poisoning. The white substance shows patchy areas of demyelination. The detail of this characteristic process, including the glia reaction, is now being studied by one of us (Ferraro) and the result of these studies will be reported later. The same applies to the reaction of the glia elements in the areas of demyelination and surrounding them.

Histological study of the kidneys reveals the presence of some infiltrative cells in the medullary substance and a diffuse shrinkage of the tissue in both cortex and medulla (Fig. 29). Shrinkage and capillary hemorrhages are found in the liver. No fatty degeneration. Congestion and spotty hemorrhages of the lungs and of the heart and liver. Hypersecretion of mucosa in the intestinal walls.

Cat Dinky—Lab. 81. Weight 4 kg.

Animal received subcutaneous injection of potassium cyanide starting with 2 mg. up to 28 mg. of cyanide. Animal was injected daily from March 8 to April 14, 1932, with the exception of March 20, March 24, April 2 and 3, and April 14. April 14, the animal weighed 3,400 grams.

Altogether this animal had 516 mg. of cyanide in the course of 34 injections.

April 12, 1932: Animal developed signs of paralysis of the hind legs, which was very pronounced at the time of his death on April 14.

Histological Study: The brain cortex reveals the same changes reported in the previous cases, i. e., a moderate cellular involvement of the shrinkage type with no disturbance of lamination. Lesions of the liquefaction type so characteristic for histamin and indol poisoning are present here and there in the most inner layer of the cortex.

The white substance shows areas of considerable demyelination, the investigation of which is forming the subject of a special study dealing with the experimental reproduction of encephalopathy of the diffuse sclerotic type. The borders of the areas of demyelination disclose reactive phenomena on the part of the astrocytes.

The pathology of the internal organs does not vary from the previous case with the exception that the walls of the small intestine show a certain amount of fatty degeneration of the mucosa and more so of the submucosa.



Fig. 29. Shrinkage of renal tubules and lymphocytic infiltration of the medulla of the kidney. H & E stain



Cat Tony—Lab. 85. Weight 4,480 grams.

Animal injected subcutaneously on April 28, 1932, with 2 mg. of potassium cyanide. At first the animal appeared restless but later became very quiet. Licked mouth constantly.

April 29, 1932: Injection of 3 mg. of cyanide. Bowel movements, vomiting, rather restless at first, then drowsy.

April 30, 1932: Injection of 4 mg. of cyanide. Same reaction as above. Marked heavy breathing.

May 1, 1932: Injection of 5 mg. of cyanide.

May 2, 1932: Injection of 6 mg. cyanide. Cat appeared very drowsy, breathing very heavily. Vomiting; convulsive seizures. The convulsions appeared three times in the space of two and a half hours and then the cat died.

Altogether this cat received 20 mg. of potassium cyanide in the course of five days.

Histological study deferred. Scope of the experiment was to establish the individual resistance to KCN.

Cat No. 7—Lab. 2. Weight 4 kg.

Animal injected on three successive days, March 4, 5 and 6, 1931, with 150 mg. of indol followed by an additional injection of 1, 1.5, and 2 mg. respectively of potassium cyanide.

March 9, 1931: 21½ mg. of cyanide were added to 150 mg. of indol. In about four minutes the respiration became markedly increased and the animal cried constantly. Five minutes later there was slight twitching of the foreleg and a little later the hind legs also showed slight twitching. Animal showed marked general muscular weakness which lasted for ½ hour during which time the animal lay on one side. During this time he had vomiting and was unable to rise. Pupils were markedly dilated and mucous membranes were blanched and the foot pads were moist. One-half hour later, when the animal resumed walking, he appeared slightly ataxic which fact may have been due to muscular weakness. Superficial sensibility, including pain sensibility, appeared decreased, whereas, the tapping of forelimbs caused contraction of hind and front limbs. The next morning the cat was found dead. Nothing different at autopsy except the cherry red appearance of the blood found in cyanide poisoning. Urine drawn from bladder showed marked indican reaction and three plus albumin. No casts but large numbers of red cells were seen.

Histological Study: All over the cortex there are diffuse degenerative changes of nerve cells in which the lesions consist of a combination of ele-

ments disclosing shrunken aspects and elements showing the acute severe type of lesion associated with more or less pronounced vacuolization and liquefaction (Fig. 30). The character of the lesion of the individual cells need not be repeated as the shrunken elements answer to the description which we have made of the cellular changes in Cat No. 10. The same applies to the severe acute lesion consisting in the usual swelling of the cytoplasm, disappearance of the Nissl body, swelling of the processes, shrinkage of the nucleus, and appearance of vacuoles in the cytoplasm. The vacuoles are generally seen first surrounding the nucleus and gradually invade the cytoplasm leading to more or less complete liquefaction of the element.

The lesions of both the shrunken and the liquefactive type are not very severe though here and there areas are found in which the lesions are more pronounced and other areas in which one or the other type of lesion predominates. With the difference in intensity the predilection of the lesions is more or less the same as the ones described in indol and indol and histamin poisoning. In the cerebellum the Purkinje elements are also involved though not so severely as in the combination of indol with histamin. The lesions consist mainly of homogenization and granular disintegration of the chromatin substance. In the spinal cord the cells of the posterior horn are particularly involved.

The astrocytes, oligodendroglia, microglia, show, though in a lesser degree of intensity and diffusion, the same degenerative changes as described in the case of indol and histamin poisoning.

Cat No. 9—Lab. 6. Weight 3,800 grams.

Animal was injected on March 13, 1931, with 1 mg. of potassium cyanide followed by 150 mg. of indol. On March 14 the dose of potassium cyanide was increased to 1.5 mg. and on March 16, 18, 19, 20, 23 and 24 the dose was increased to 2.5 mg. of cyanide, always associated with 150 mg. of indol.

March 18, 1931: Twitching of facial muscles started in 10 minutes but were fleeting in character. There was hypersensibility and increased respiration with an attempt to vomit. Paling of the mucous membrane and salivation.

March 20, 1931: Vomiting appears in 10 minutes following injection. Animal is hypersensitive to outside stimuli and shows marked muscular weakness especially in the hind limbs. Respirations are still markedly increased after one hour. Cat lies limply on side panting for breath. Mucous membranes of mouth very pale. At autopsy on March 26 bloody urine was

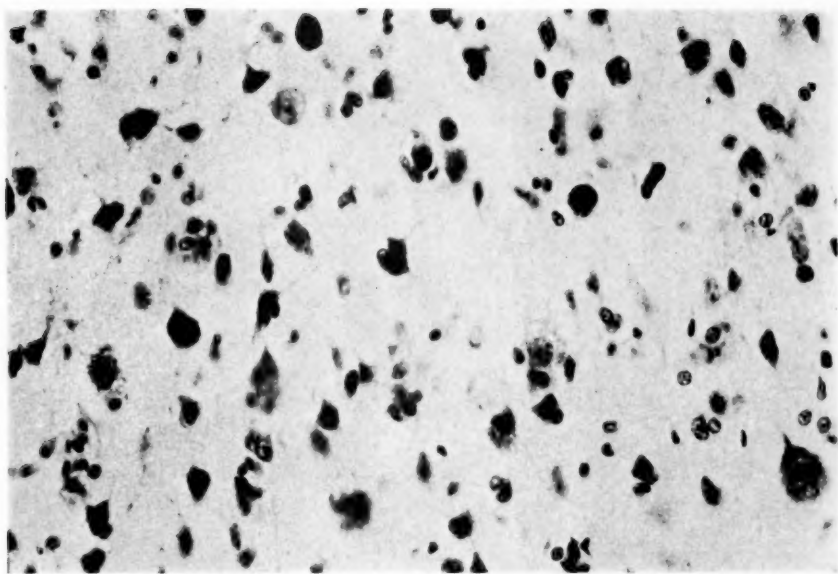
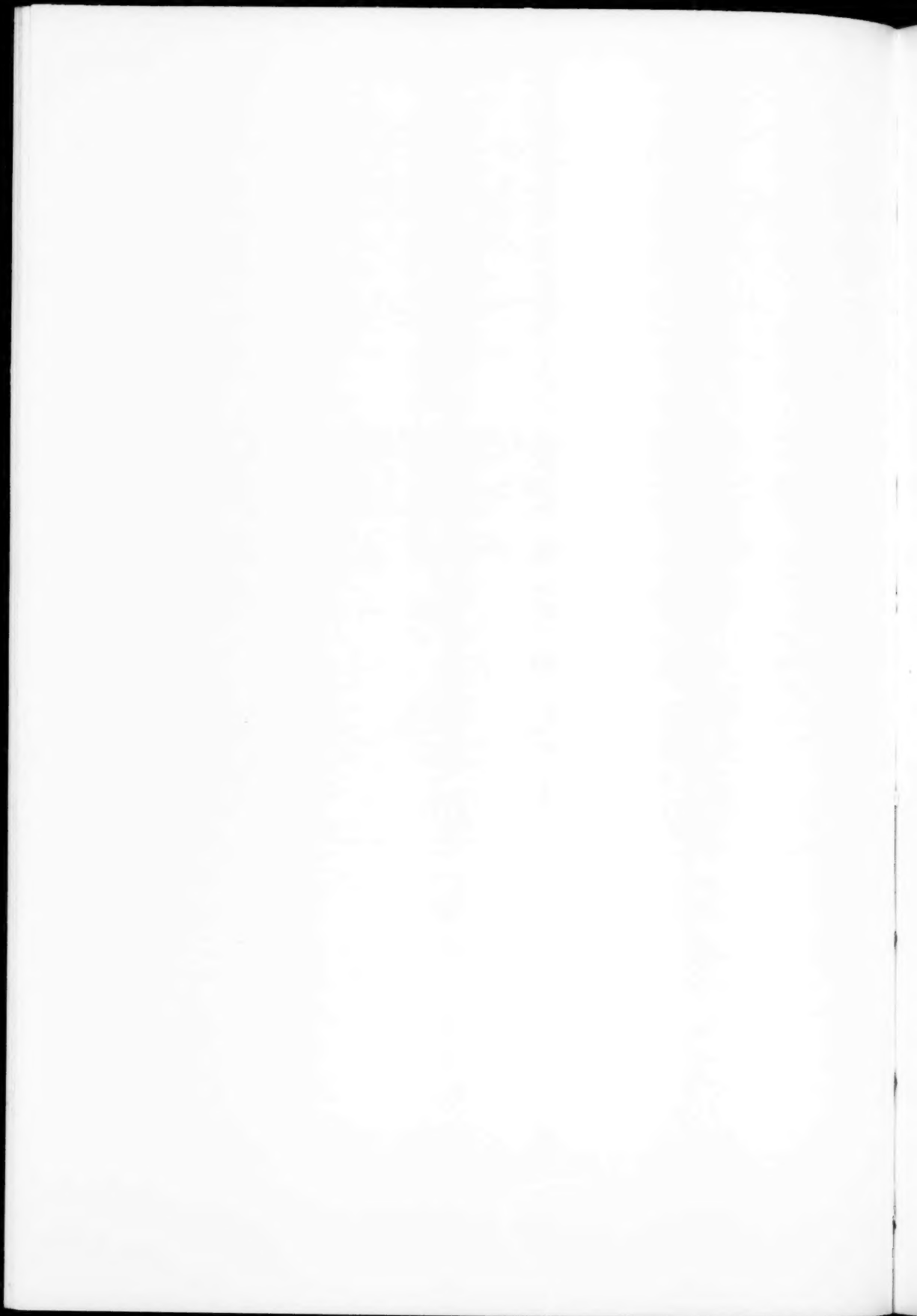


Fig. 30. Nerve cell change represented by combination of shrinkage and acute degenerative change. Nissl stain for nerve cells



found in the bladder and serous fluid in thoracic cavity and abdomen. Lungs slightly edematous. Otherwise no gross pathology of the organs.

Histological Study: The changes are comparable to those described in Cat No. 7 and consist mainly of diffuse degenerative changes of the nerve cells scattered all over the cortex and represented mainly by the severe type of degeneration taking place through a more or less pronounced process of vacuolization and liquefaction. Intermingled with the swollen degenerated elements shrunken nerve cells are seen comparable to those found in poisoning with potassium cyanide alone. The lesions extend in the brain stem and in the cerebellum where both Purkinje elements and the layer of the granules are involved. The lesions involving the astrocytes are of the same nature as those described in the previous animal though slightly more severe and here also consist in the degenerative changes of these elements, swelling of the cell body, of the processes, and deformity and breaking down of the same. The oligodendroglia show acute swelling in both gray and white matter, while the microglia undergo also slight degenerative changes represented by swelling and deformity of the cell body and processes with slight homogenization of the cytoplasm.

Cat Blackie—Lab. 83. Weight 3,100 grams.

This animal was injected on March 17, 1932, with 150 mg. of indol in addition to 3 mg. of cyanide. The dose of indol was kept constant daily while the KCN was increased on March 22 to 4 mg. and on May 24 to 5 mg.

Animal died on April 25 after 39 days from the beginning of the experiments. This cat shows again the importance of the individual factors in the resistance to experimental poisoning.

Cat Pluto.

On this cat weighing 3 kg. an experiment has been started to investigate the action of cyanide and histamin. On March 8, 1932, animal received 10 mg. of histamin (aqueous solution prepared in our laboratory) associated daily with 5 mg. of potassium cyanide.

May 9, 1932: The animal is now getting very sick.

COMMENTS

A point on which all our experiments are in accord is the evident reaction of the nervous tissue to the damaging effect of endogenous poisons such as histamin and indol which are normally found in the gastrointestinal tract. The first question which comes to our mind is the one dealing with the amount of toxic substance necessary for

the setting up of such a pathological reaction in the brain. We must here remember that according to Herter one may find as much as 50 to 60 mg. of indol in 100 grams of fresh stool. This, as already mentioned, probably approaches the maximum amount present at any one time. If we consider the daily output of stool as between approximately 500 and 1,000 grams, a quantity of indol between 500 and 600 grams could therefore possibly be found in daily excretion. It is presumable that another amount of indol remains in association with materials still retained by the gut which fact may considerably increase the total amount of indol which might at one time or another be present in the gastrointestinal tract. Considering the average weight of the human individual to be 60 kg. and the average weight of the cats used in our experiments to be 3 kg. it follows that to obtain the same deadly result in man, provided that man reacts in the identical manner as the cat, a daily dose of 2,000 to 3,000 mg., repeated over periods of weeks or months, would be necessary by subcutaneous injection, corresponding to daily doses of 100 to 150 mg. received by the cat. Undoubtedly such an amount is excessive and up to now has to be considered far greater than the maximum amount of indol found in human feces. But the above-mentioned dose would be of particular interest only if death were considered as the ultimate and the only result which might be expected from the action of indol on the human organism. But if we consider that a pathological action, though not very severe, of the drug on the nervous tissue, may be the result of much smaller doses, we understand the importance that such small doses, especially when acting over very long periods of time, may play in involving the structures of the brain and possibly influencing our mental processes.

If we now consider that in the presence of pathological changes involving the protective mechanism (liver, lungs, intestines) indol may be less completely detoxified, we feel that under such circumstances even smaller amounts of indol would be found to be detrimental to the nervous system.

The same applies to histamin. How much histamin is normally found in the human body? According to Hanke and Koessler they were able to get from 6 to 20 mg. of histamin yield in from 500 to

600 grams of normal human feces. Though this amount if isolated might not result in a rapidly damaging effect on the central nervous system, its presence may be of great importance in connection with its association with other toxic substances found in the gastrointestinal tract, mainly indol.

And here, therefore, enters into consideration the second important factor represented by the association of more than one toxic element in determining the intensity of the pathological changes.

It has been said previously that in the presence of small amounts of histamin, (as low as 3 mg., that is, an average of 1 mg. per kilo weight of the animal) the toxic effect of indol appeared to be more pronounced and more rapid. The dose of 1 mg. per kilo as an average would necessitate under the same circumstances, if a comparison may be made between human and animal resistance, the presence of between 50 and 60 mg. in man to produce the same damaging effects. If we consider Hanke and Koessler, who found as much as 50 to 75 mg. of histamin per kg. of feces in man, it is logical to assume that such an amount is sufficient in man in association with indol to produce the toxic results which have been experimentally reproduced in animals.

In our experiments the total amount of indol necessary to produce death in one of the cats—Cat No. 6, for instance, which received daily doses of 150 mg.—is 12,250 mg., injected in 76 injections, with death occurring in 95 days. If, however, histamin is associated with indol at the daily dose of only 3 mg., the total amount of indol required to produce death of the animal has been reduced in one instance to 1,350 mg., a reduction of practically 9/10 of the previous dose, with death occurring 11 days after the beginning of the experiment.

Not in all the animals has the association of these two drugs worked so drastically but in all of them the association of histamin and indol undoubtedly shortens the duration of the animal's life and aggravates the pathological changes detectable in the brain tissue. We must not forget here the possibility that in the future more appropriate and more delicate biochemical methods may allow us to detect indol and histamin in circulation in an easier and more accurate way than we are now able to do. This fact might

allow us to take the indol or histamin content of the blood or of other fluids (cerebrospinal fluid) as a better index of the amount of the toxins circulating at a certain given time.

At this point we must take into consideration the element represented by the individual resistance of the animal investigated. It is a fact that even taking into account the factor of weight, substantial differences have been found in various animals as to their resistance to the administration of combinations of toxic substances. This variability applies not only to indol and histamin combined but extends also to the use of KCN alone, which in some instances can be administered for a rather long period of time before death occurs, whereas in some other instances the resistance of the animal to the same proportionate doses is considerably less pronounced.

We unfortunately have no way of determining beforehand the individual resistance of a given animal to the associated action of two drugs and will therefore have to rely, in establishing the importance of such association, on the severity of the pathological process derived from the combined action of more than one drug. For instance, we know of the resistance of the majority of our cats to the daily dose of 100 mg. of indol injected subcutaneously and we know that doses as high as 5 mg. of histamin can be injected for periods of months without damaging severely the nervous tissue. The moment, however, that 100 mg. of indol are associated with 3 mg. of histamin, the lesions resulting from this association are very severe and certainly definitely in contrast with the mild lesions following the use of either histamin or indol injected alone in the same amount.

The same applies to KCN. Though there is undoubtedly a variation due to individual resistance, the type of lesions following association of KCN and indol is certainly of a different nature than those described following the use of KCN alone. It follows that the severity of lesions produced by the association of 150 mg. of indol, which by itself would not result in severe pathological changes, in the space of 4 or 6 days, can be used as an index of the importance of the association of indol with KCN in the determination of the severe changes reported.

Of course the factor of time must also be taken into consideration when the data relative to animals are referred to man. It requires, in other words, the continuous association of indol and histamin in order to produce the severe changes which we have described histologically in cats. In Cat E, for instance, the association of indol and histamin had to be prolonged for 40 days in order to produce death of the animal and in Cat No. 8, 33 injections of indol were accompanied by 16 injections of histamin before death occurred in 49 days. It seems, therefore, that a certain constancy of the association of the two drugs is required over a certain length of time before fatal damages may result. It is possible, however, that in man finding of an association of indol and histamin may not be as constant as one reproduced experimentally, which fact may account for a different type of reaction. It may also be possible that either one of the two substances may be present at one time and absent at another, therefore making the final result occur at longer intervals of time. There is a suggestion, in fact, in our experiments that if the association of indol and histamin is not a daily one, the life of the animal is prolonged over a longer period of time than if histamin is given in a daily association with indol or if indol is given in daily association with histamin.

Still another factor to be taken into consideration is the one dealing with the direct presence of histamin in various organs. As shown by various authors histamin can be extracted from the kidney, spleen, liver, muscular tissue, glandular tissue, gastrointestinal mucosa, etc. The presence of histamin in the liver and in the mucosa of the gastrointestinal tract is of particular importance because of the role played by both of these organs in detoxifying indol. As shown by our experiments, Cat A, for instance, the continuous use of histamin alone, though in small amounts, may result in a fatty degeneration of the liver, which fact may account for a diminished protective function of this organ in the oxidation of indol or other toxic substances. In the association of histamin and indol intoxication, the histamin might play the part of predisposing agent by severely affecting the functionality of the liver cells. The opposite action of indol predisposing to more damaging effect on

the part of the histamin might not be as important because of the less severe changes of the liver in intoxication with small doses of indol. According to Biebl, who particularly studied the pathology of the various organs following acute, sub-acute and chronic indol intoxication, the main lesions are found in the kidneys. On the other hand, Metchnikoff and his pupils, E. Wollmann and S. Drat-schinski, found following administration of paracresols and indols in rabbits, rats, and monkeys some athromatous changes and some interstitial inflammatory changes in the liver.

In our series of animals poisoned with indol alone we have also found considerable damage of the liver when high doses of the drug were used, whereas histamin affects the liver structure even in small doses. It is justifiable, therefore, to hypothecate a possible predisposing action played by histamin in paving the way to more severe damage of the nervous system when another toxin enters into action, though indol might to a lesser extent play the same pre-disposing role for other substances.

It follows that the question of how the two drugs in association increase their toxicity is not as yet solved as it might also be that besides the individual action of each drug over organs, the normal function of which is essential for detoxication and therefore for the protection of the central nervous system, the simultaneous introduction of two different drugs in the circulatory system may lead to the creation of a third toxic product the action of which might be more severe. Chemical investigations along these lines are suggested.

On the other hand, if we recall the physiological action of histamin as a depressor agent accompanied by vasodilation and increased permeability of the capillaries, we may more easily understand why toxic substances injected in association with histamin administration may reach the general circulation more rapidly and in a larger amount.

In discussing the question of dosage we must also take into consideration the fact that though clinical neurological manifestations may be absent, mental changes may occur which in the animal may escape our means of investigation. As a matter of fact, no attempt has been made in our cases to correlate slight histological changes

with changes in the behavior of these animals as established prior to, during, and after, the experimental poisoning. There is here a suggestion of amplifying our experiment by studying the behavior reaction of animals for several months before the animals are put under the action of toxic substances and to compare these reactions with those following a more or less prolonged period of experimental intoxication. It is obvious that the factor of physical disability will have to be taken into account in order to differentiate, if possible, the changes in behavior due to central nervous involvement from the ones which might be apparent only and due to the general weak and unhealthy condition induced by the toxic substances.

* * *

We have discussed in our paper the protective action which the intestinal mucosa seems to play in detoxifying indol. The integrity of the intestinal mucosa is, therefore, a pre-requisite for the protection of the nervous system from the toxic effect of such a drug.

In this connection pathological changes occurring in the intestinal mucosa must play an important role in the ability of the intestinal mucosa to oxidize indol and to pair it with sulphuric acid. This is why the pathological study of the gastro-intestinal tract already reported by Cotton (1921)⁸⁸ is of considerable importance.⁸⁹ The lesions which this author reports in cases of mental disease "vary from isolated chronic punched-out ulceration to diffuse enteritis with serious damage to the entire mucous lining epithelium. When the infectious process had persisted for years the colon was found to have lost its normal appearance and reduced in some cases to only a thin membrane in which the muscular and epithelial coats had been entirely destroyed. In these thinned-out sacs the putrefying bowel contents have been proved by the X-ray to have remained as long as 10 days pouring toxic bacteria and all forms of poisons into the patient's system."

The same inflammatory changes were reported by Ludlum in the intestinal mucosa of mental cases and congestion and atrophy of the mucosa described by Bolsi in few mental cases. Snessarew reports also inflammatory changes of the intestines in nine cases of dementia præcox and we all are familiar with the extensive mono-

graph of Reiter dealing with the dysfunction of the gastrointestinal tract and the pathological changes found in the intestines of schizophrenics.

In Italy, Buscaino's pupils, and collaborators Roberti, Mazzanti, DeGiacomo, Noto, Gullotta, have been emphasizing in the last few years the importance of pathological changes in the gastrointestinal tract as well as in the liver in mental diseases in order to substantiate Buscaino's contention that dementia præcox is due to the action of an abnormal amine (histamin) circulating in the blood and reaching the circulation because of an insufficient hepatic and intestinal protective barrier.

The pathogenesis of the changes in the gastrointestinal mucosa might to a certain extent be found in the action of indol or histamin over the intestinal walls of both large and small intestines. Important also in the pathogenesis of lesion of the gastrointestinal mucosa may be the presence of infectious agents in the gastrointestinal tract and, therefore, from this standpoint the question of intoxication and infection might become to a certain extent closely correlated.

Concerning the liver pathology, very little is known as to its cause. It is possible, however, that toxic substances such as indol and histamin may directly harm the liver structure and such a contention seems to be supported by lesions of the liver found in our experimental investigation when histamin or indol alone were used by subcutaneous injection. At any rate, once the lesions are established it would seem natural that they might interfere especially in the process of oxidation of toxic substances. We have already mentioned in our introduction the views concerning the importance of the screening function played by the liver against injurious action of the indol circulating in the blood. Concerning histamin, though the action of the liver is of a certain importance, it seems that the detoxifying action of the intestine is also very important.

At any rate, investigation of the liver function and the histological study of the livers belonging to cases of mental disease have centered the attention of many investigators on this problem. Out of 75 livers of dementia præcox which have been histologically examined by various authors (Dunton (1904), Laignel-Lavastine

(1905), Benigni and Zilocchi (1908), Claude and Rose (1908), Parhon (1910), Marie and Dide (1910), Obreggia, Parhon and Urechia (1913), Orton (1913), Von Klebesberg (1914), Gargiulo (1914), Mazzini and Vidoni (1914), Buscaino (1922), Bolsi (1925), Mazzanti (1926), Roberti (1927), Reiter (1929), etc., 90 per cent of them showed chronic and degenerative type of involvement, which fact makes it presumable that a dysfunction of the liver might be translated into the presence of toxic substances in the urine.

In 1929, Gullotta, a pupil of Buscaino, made a very careful investigation of the liver functionality of mental cases by the study of the liberation of the biliary pigments, the metabolism of sugar, and the protein metabolism. He reported extensively all the work that has been done by various authors as Mongeri, Butenko, Leyser, Schrijver and Buchler on the study of biliary pigments, that is, urobiline and bilirubine, and emphasized the fact that Buchler in 86 cases of schizophrenia found in 40 per cent hyperbilirubinemia and in 85 per cent urobilinuria. Scheiner in 35 cases of amentia in the sense of "frenosi sensoria hallucinatoria" reported also 100 per cent of bilirubinemia and out of 31 dementia praecox cases, 57 per cent of the same condition.

The metabolism of the carbohydrates as a test for liver functionality was carried by numerous authors (Duse, Muggia, Ehrenberg, Schultze and Knauer). Heidema found in 10 out of 13 cases of dementia praecox hyperglycemia of the blood. A high percentage of hyperglycemia has also been reported by Uyematsu, and by Soda in 47 per cent of the cases. Lorenz found also alimentary and spontaneous hyperglycemia in catatonia. DeGiacomo, in 30 cases of dementia praecox, found 19 with slight hyperglycemia. Hypoglycemia was on the other hand found by Ganzel, Dide and Pages and by Forest Smith and Gardiner Hill.

Acetonuria has also been used as an index for liver insufficiency and Shaw in cases of amentia and Palmer in cases of dementia praecox reported acetonuria leading to acidosis.

Insufficiency of the liver function as detected by the nitrogenous metabolism has been worked by Mongeri who found a diminution of urea, by Pighini who found a retention of nitrogen, by Hayashi who reported a diminution of urea. Diminution of uric acid con-

trasting with normal total nitrogen urea and creatinine is reported by Uyematsu and Soda. Walker, in 28 schizophrenics, found that concomitantly with diminished residual nitrogen in the blood there was a diminished elimination of urea in 57 per cent of the cases.

McIntyre, in 18 cases of amentia noted retention of nitrogen in addition to a state of acidosis. Thomas, basing his investigation on the occurrence of acidosis as demonstrated by Shaw by the presence of acetonuria has studied the alkali reserve and alkali tolerance in cases of mental confusion and confirmed the existence of considerable acidosis in some of the cases.

Gullotta has added to the study of the liver functionality the exploration of its chromagogue function by the method of the Rose Bengal, of Fiessinger and Walter, consisting in the study of the retention of a dye injected into the blood. In order to exclude that increase of billiary pigment in the blood might be the expression of a hemolytic process, Gullotta has studied the globular resistance of the blood. From the conclusion of his work, it appears that a hemolytic process does not occur and that in all the 12 cases of amentia which the author examined, there was an increase in the amount of retention in the blood of the Rose Bengal which constitutes the so-called aromatemia. In the urines of these patients with a positive Buscaino reaction he also always found aromaturia and a positive reaction for indol, scatol, uroroseine, and a positive reaction of Millon. In some cases positivity of the diazo-reaction of Ehrlich, of the reaction of Weiss, and lowering of the superficial tension was found.

In 25 cases of dementia præcox the results of the author may be divided into two groups. In one group, the group of the recent cases or in cases of relapse, the results were analogous to those reported in amentia (aromaturia plus aromatemia), whereas, in the group of long standing cases such reactions did not occur.

According to Gullotta the analogy of the behavior of the cases of amentia with early cases of dementia præcox, in a stage of confusion or stupor, suggests the like genesis of these conditions, whereas, the appearance of the aromaturia concomitantly with the aromatemia upholds the toxic-enterogenic origin of amentia advocated by Buscaino.

In 1930, Noto, another pupil of Buscaino, following Gullotta's experiments of administering by mouth one-half gram of tyrosin with subsequent appearance of aromatic substance in the urine and in the blood of dementia præcox, contrasting with the absence of aromatemia in a normal control, extended Gullotta's investigation to 20 cases of dementia præcox and found that the presence of aromatic substance of the phenol series were positive in 90 per cent of the cases of dementia præcox and in only 33 per cent of the controls. Noto's explanation of this fact is that in the intestines of the dementia præcox abnormal putrefactive processes take place splitting the tyrosin and liberating, therefore, the abnormal products with a phenolic structure. Because of the existence of lesions of the gastrointestinal mucosa and of the liver these abnormal products are allowed to pass into the circulation.

* * *

The fact that the administration of potassium cyanide in some of our animals rendered indol much more toxic, as pointed to by the shorter duration of the experiment leading to death of the animal and more severe pathological lesions of the central nervous system, seems to us a point in favor of the necessity for indol to undergo a normal oxidizing action in the human organs. It is known, in fact, that potassium cyanide interferes considerably with the oxidizing capacity of the cells in general and our findings confirm the suggestion of A. N. Richards and J. Howland, who, because of the power of potassium cyanide in depressing the ability of animal cells to take up oxygen from the blood, feel that this substance interferes with the normal oxidation of indol.

The interference of KCN with the oxidizing capacity of the cells seems to receive some support from a few experiments which we have carried on and during which we have placed the animals under the action of KCN in an oxygen chamber where oxygen was freely administered. The animals which following KCN were breathing heavily, panting, and lying on the floor, in a few minutes after their exposure to oxygen improved considerably, respiration became normal, and their behavior appeared essentially normal. If the animal was removed from the oxygen chamber, a few minutes later the clinical symptoms already mentioned as due to the action of KCN reappeared.

* * *

The present experimental work, of which only the preliminary results are now being published, represents just an initial step toward putting the problem of the pathogenesis of mental diseases on a sound experimental basis.

The clinical justification of the experimental approach has been furnished to us by the opinion of competent psychiatrists as to the existence of psychoses, the development of which follows or is at least concomitant with autointoxication, of gastrointestinal origin. The fact that our experiments have demonstrated the existence of pathological changes in the central nervous system following the use of enterogenous toxic substances, considered at the base of the process of autointoxication, makes justifiable our contention that the nervous symptoms which develop in man following the experimental use of these toxic substances (indol and histamin) may be related directly to pathological changes occurring in the central nervous system.

Our contention of a direct relationship between these clinical symptoms and the occurrence of autointoxication from gastrointestinal toxic substances is supported by the favorable results on the mental symptoms, which in some instances follow the medical treatment of gastrointestinal conditions. It is also enhanced by the increasing reports of mental pathology, particularly dementia præcox and acute hallucinatory confusional psychosis with concomitant signs of pathology of the gastrointestinal tract and of the liver, organs which as we have noted above represent an important link in the detoxifying system of the human organism.

It is far from our mind to conceive that all mental conditions have the same etiological factor, but we feel justified in recognizing the existence of cases of mental disorders which have as a basic etiological factor a toxic condition arising in the gastrointestinal tract.

* * *

There are many important points that will have to be elucidated in connection with this experimental problem. There is, among others, the one dealing with the more detailed mechanism of action of two or more drugs when associated; there is the one dealing with the pathogenesis of the reported toxic changes in the brain if

primary or secondary to the lesions in the protective organs; there is the one dealing with the importance of the flora bacteria on the chemical content of feces; the other important one dealing with the absorption of the intestinal mucosa in normal and pathological conditions; the one dealing with the influence of lesions in glands of internal secretion or in the various detoxifying organs (liver and intestine) in decreasing the resistance of the body to the influence of endogenous toxins; there is the one dealing with the investigation of the tonus of the vegetative nervous system in connection with the severity of the toxic changes; finally from the therapeutic standpoint mention must be made of the point of how, along the lines already followed by Kopeloff,⁹⁰ to influence bacteriologically or chemically the gastrointestinal content and what most appropriate diet might eventually result in a smaller amount of protein cleavage under experimental conditions.

Moreover, no attempt has been made in our experiments to correlate severe and slight changes occurring in the central nervous system with changes in the behavior of the animal following the acute and chronic intoxication. There is here a suggestion of amplifying our experimental investigation by studying with the collaboration of a psychologist the behavior of animals for several months before the animals are put under the action of toxic substances and to compare these reactions with those following a more or less prolonged period of experimental intoxication. All these problems will require time and we hope to be in a position to report on them some time in the future.

For the present the scope of our present investigation is to call the attention of psychiatrists to the important rôle that enterogenous substances may play in the determination of toxic changes in the central nervous system, especially when more than one drug is called into action, a situation which evidently must be a common one in the gastrointestinal tract. By paying more attention to toxic agents as an etiological factor in some mental conditions the way may be paved for a better evaluation of the therapeutic measures apt to relieve the unfortunate sufferers from mental diseases, an aim which is in the heart of every psychiatrist irrespective of the school to which he belongs.

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BOOK REVIEWS

Hydrotherapy in Hospitals for Mental Diseases. By REBECKAH WRIGHT, M. D. Foreword by James V. May, M. D. Cloth. Pp. 396, with 92 illustrations. The Tudor Press, Inc., Boston, 1932.

As the first volume to be published on hydrotherapeutic procedure exclusively devoted to the treatment of psychotic cases, this book renders available much-needed information.

The subject material is divided into four sections. The first and most detailed is an instruction for nurses, instructors and hydrotherapists in the administration of the water treatments that are usually prescribed in hospitals for mental diseases. The technique of hydriatic procedures including the general and local application of heat and cold (and their physiological effects), neutral applications, irrigations, douches, revulsion and friction are presented in concise detail.

Instruction to hydrotherapists in accurate recording and in the management of the hydrotherapy department is given in the second section.

Part three reviews indications for this type of treatment with emphasis on the importance of specific prescriptions, lists the essentials for success and discusses the therapeutic effects of hydriatic applications. This section should be of especial assistance to the physicians who prescribe hydrotherapy for mental cases.

The last section deals particularly with the construction of hydriatic suites, emphasizing the value of planning the building around the treatment, and will be of particular interest to superintendents of hospitals for mental diseases.

The book as a whole is concise in definitions and exhaustive in range. It embodies the attributes of simplicity in style, conciseness of thought and facility of expression that will make aspects of this work which are sometimes difficult for the beginner, easy to comprehend. It will serve to orient the more experienced psychiatrist in hydrotherapy because its pages include only data relevant to his specialized field. It is, further, designed to be of use to instructors in training schools, constituting material for a course of lectures and demonstrations to student nurses.

Physically, this book makes an excellent impression.

LYBYER.

What Becomes of the Children Removed from Home by Oslo Child Welfare Board? A Statistical Study Based on Experiences of Oslo Child Welfare Board, 1900-1928. By SIGNY ARCTANDER and SIGURD DAHLSTRÖM. Published by Child Welfare Board, Oslo, Norway.

In any field of endeavor a thorough analytic study of the fruits of one's labor is of paramount significance. It is only through a careful evaluation of the end-result in relation to the continuing process that a causal relationship may be definitely established. Accumulated data for a period of 30 years of experience of the Oslo Child Welfare Board forms a basis for the statistical analysis of the results achieved.

The study is concerned with the results of the work of the Child Welfare Board as reflected in the adjustment of children after discharge. Adjustment is measured in terms of the proportion of persons sentenced, the number of individuals repeatedly convicted, those convicted and receiving poor relief, and occupational status. The actual investigation is concerned with 2,762 individuals (1,800 boys and 952 girls) who were removed from their own homes from infancy to 17 years; the age range of the discharged group at the time of the investigation was from 15 to 40 years. In this statistical analysis, precaution was taken to compare the degree of adjustment of children for similar after-periods, i. e., the amount of time that had elapsed since discharge from active supervision.

The findings indicate that 32.9 per cent of the boys and 4.8 per cent of the girls were convicted of offenses after being discharged from the care of the Child Welfare Board. The relatively small percentage of girls convicted of offenses cannot easily be explained although the maladjustment of girls may often assume the form of criminality which may not result in actual sentences.

It will be observed that nearly one-third of the boys were convicted of offenses after discharge. It is not possible to say whether this proportion of convicted persons reflects favorably or unfavorably on the work of the Child Welfare Board. Comparisons would have to be made with the results obtained for similar groups of children who were not removed from their own homes but were allowed to drift in their respective environments without the assistance of a social case work agency. Still another control group might be employed comprising similar problem children who were supervised in their own homes by a social agency or placed under court probation. Such comparative data would cast some light on the advantages accruing from the removal of children from their own homes.

As a result of elaborate statistical treatment of the data the authors ar-

rived at the conclusion that children who are removed from their own homes at an early age and placed under supervision of the Child Welfare Board are less likely to develop criminal tendencies in later life than those removed from their homes at a later age. Thus, of the boys removed from their homes prior to the age of 8 years, 12.3 per cent were afterwards convicted, while of those removed after the age of 8 years, 36.2 per cent were sentenced. The corresponding figures for girls were 1.4 per cent and 6.3 per cent. Also, the percentage of convictions for those removed after the eighth year increased sharply according to the age at removal, the maximum percentage of convictions (45 per cent) being reached for those removed at the latest age. These results would seem to indicate that the time of intervention of social agencies on behalf of the child is an important factor in the prevention of delinquency.

These results evoke a fundamental question in the field of child care. At what age should a child be removed from an unfavorable environment? The statistical analysis indicates that there is no marked difference in the percentage of convictions for ages (at the time of removal) up to eight years but after this period the percentage of children convicted increases with an increase in age at the time of removal. However, it is quite possible that the younger children who were removed by the Oslo Child Welfare Board comprised in the main neglected children who had not yet exhibited aberration of behavior, while those removed after the age of eight years had already been stamped by society as delinquent. Also, those children who were removed at an early age generally received a longer period of supervision than those removed at a later age, so that the duration of supervision and not the age of removal from home may have been the determining factor in the later adjustment.

The scope of this study embraces some of the most fundamental problems in the field of child-care. Although the factual material is concerned with the Oslo Child Welfare Board, the existence of similar social agencies in various parts of the world suggest common problems irrespective of varying social and economic conditions. The results of the investigation are very illuminating and the utmost precaution has been taken to formulate only those conclusions that are warranted by available facts. From the standpoint of methodology and statistical treatment, this work is indeed stimulating. The findings in the study should prove of particular importance to social agencies, educators and all those who manifest an interest in the manifold problems of child-care and juvenile delinquency.

ROBERT AXEL.

Clinical Lectures on Psychological Medicine. By HENRY YELLOWLEES, O. B. E., M. D., Physician for Psychological Medicine, St. Thomas' Hospital, London. Printed in Great Britain, 1932, 12s 6d. J. and A. Churchill.

Most of these lectures were delivered to students at St. Thomas' Hospital, a few at medical meetings and some were written especially for this book. They are elementary in character, for the most part; contain material not readily accessible, and so will appeal to the general practitioner as well as the student. The chapter on, "Suggestion and Persuasion" was taken from the author's "Manual on Psychotherapy."

As he states, the lectures are, "an attempt at a return to that clinical approach which is the foundation of all sound medical teaching and is nowhere more essential than in psychiatry," and are intended to be studied along with a course of clinical demonstrations. The reviewer believes the book of immeasurable service to young men starting out in institutional work.

Classification is not stressed, emphasis being placed on symptomatology and treatment. The first chapter, naturally, introduces the study of psychiatry, but especially the method of approach to the individual patient. Here he presents many admirable suggestions on the best way to develop a satisfactory relationship between himself and his patient. His style is simple but dignified and holds one's interest. "We should talk to the insane, generally speaking, as if we were talking to the sane. We can never go far wrong, if we do that, provided, of course, that our talk to the sane is worth hearing." "Almost as important as the art of talking wisely, is that of listening wisely." These quotations are typical of his paternal manner of gently bringing us to the details of symptoms and treatment.

Without selecting any typical psychosis to illustrate the general states in mental disorders, he describes depression, elation, delirium, etc., with the ease of a master. One can almost imagine himself again a student in the amphitheater, under the spell of a lecturer, commonplace in dress possibly, but with a dynamic, forceful personality, who brings out the points so clearly they stand out cameo-like.

The various chapters gradually carry one through the recognized forms of mental disorders, but one does not meet paresis and other organic conditions singled out for specific treatment in separate chapters, as we do in books on this subject generally. Instead the author brings them out in connection with points as he develops each lecture. The book is, therefore, not so useful in a reference library.

Separate lectures that appealed to the reviewer include the very practical

introductory one on the manner of approach, those on states of depression and elation, a study of delusions and the "Psychoses and Psychoneuroses Contrasted."

The volume is well made and well dressed, the paper of good quality, with a dull surface, so it is not tiring to the eyes. Headings on each page and an index afford a quick reference to the different clinical essentials and entities. Careful attention to his valuable suggestions, coupled with practical application on the wards of a state hospital ought to qualify one to quickly understand psychological medicine.

GRAY.

Problems in the Training of Certain Special-Class Teachers.

By LOUIS M. SCHLEIER, Ph. D., Contributions to Education, No. 475. 138 pages. \$1.50. Bureau of Publications. Teachers College, Columbia University.

For this study an immense amount of information has been collected from a large variety of sources. Analyzed and clarified by many tables, it is here presented in remarkably small volume for such a comprehensive survey. In his introductory chapter the author states that he "seeks (1) to present a digest and an analysis of the laws of the several states pertaining to the education and training of mentally-handicapped and physically-handicapped children in the public schools; (2) to give the rulings of state boards of education relative to the preparation of teachers for such classes and to evaluate these rulings in the light of plans suggested by expert students of special education and by selected teachers in the field; (3) to make a survey of courses and curricula now offered in the various institutions of higher learning for the preparation of teachers and supervisors of special classes and (4) to propose a teacher-training program for teachers of mentally-handicapped and physically-handicapped children in the public schools."

The author's report of the state laws is very illuminating and would seem to show that there is much room for improvement in the field of education of handicapped children. At the present time only 16 states have laws regarding the establishment of classes for the mentally handicapped, and of these states only five make it mandatory for the school board to establish classes. In addition many of the existing laws are inadequate and provide for only one type of handicapped child. Iowa chooses the deaf for special favor and Kentucky the partially sighted.

Surveying the state board requirements for teachers of special classes,

Dr. Schleier finds that in general the standards formulated concerning general educational requirements prior to technical training are satisfactory, but the technical training itself and the required amount of previous experience in the regular grades is inadequate.

A study of the courses for the training of special teachers shows that little constructive effort is being made in this respect at present, only 12 institutions in the country having established departments and definite curricula for teachers and supervisors of special classes.

The author's conclusions and recommendations are clear and concise. Agreeing with other authorities, whom he cites, Dr. Schleier feels that the proper place to train teachers of handicapped children is a professional school for teachers. He recommends that all persons who desire to become candidates for special class certification shall have had, following graduation from high school, not less than two years of preparation for teaching in the elementary school, and a minimum of two years teaching experience in the elementary grades, preferably in grades one to six inclusive. He emphasizes the necessity for selecting the candidates who have desirable personal qualifications, among which he mentions sympathy, cheerfulness, love for the work and good health. The author believes that a course for special class teachers should be at least two years in length and consist of a general program in the first year, while the second and final year should be devoted to specialized training for the particular branch of the work that the candidate has chosen.

An excellent bibliography is appended, and this interesting work, though its appeal is naturally somewhat limited, should form a very valuable reference on the subject of special education.

PATRICIA STEEN.

Nervous Infections of the Central Nervous System. Twenty-two chapters by various authors. 532 pages. Williams & Wilkins Company, Baltimore.

This volume contains all the papers read before the Association for Research in Nervous and Mental Disease at its meeting in December, 1931. The principal topics dealt with are poliomyelitis, epidemic encephalitis and meningitis. The authors are all investigators of repute. The book is amply illustrated with splendid photo-micrographs. There is a discussion after each section and an extensive bibliography. This book is recommended as a thoroughly scientific treatise on infections of the nervous system.

J. L. TOWER.

Parenthood and Civilization. By GEORGE H. DONAHUE, M. D. 74 pages.

Price \$1.50. The Christopher Publishing House, Boston, Massachusetts.

With evangelical fervor the author of this thesis seeks to prove "the necessity of *incarnating the cosmic law* of Dynamo-Genie Continuity in every developing phase of human being and becoming." He feels that all our woes are due to the recognition of a finite distinction between the material and the ideal. To prove that this distinction is a "Delusion" he devotes 31 of his 74 pages to a florid recapitulation of advances in chemistry and physics beginning at the time of Aristotle and ending triumphantly with a description of Sir J. J. Thomson's work on the atom. Thomson's discovery of the electrical charge of the particles of the atom, leads Dr. Donovan to exclaim ecstatically "We live in a cosmos: We are cosmically conditioned! . . . We are not only broadcasters of electro-magnetic waves emanating from our *selves*, but also receivers of electro-magnetic waves which emanate from things constituting our cosmic environment by which we are moved to endeavor to realize the potentialities transmitted to us as *our sole birthright*." According to the author the solution of all world problems lies in awakening children "To the stupendous significance to self and to civilization of their acquisition of this something which can be only self-acquired—a sovereignty within themselves, a selfhood, a personality—self-knowing, self-directing, self-controlling, self-reverencing."

The author heartily condemns indoctrination as "the most monstrous of all possible crimes," refers to the Golden Rule, and tells us we must inspire our children to aspire "to be and to become." The author's unique literary style tempts one to quote further. "Conscious concomitance of every aspirational effort toward supremest correlation and integration of the dynamo-genically related processes and products of the human organism, and, as such, its most stabilizing and enhancingly directing agency, deepest rooted in knowledge and understanding yet nascently transcending both, untinted in the slightest degree with credulity yet linked indissolubly with the inscrutable mystery underlying everything phenomenal and mutable—FAITH, not improperly so called, is that ever enhancing product of a personal synthesis of intellect and of emotion whereby motivations are to be freed from mere immediate sensuous self-seeking, the human organism maintained attuned to every assimilable phase of the process of the cosmos, to the end of being in unison with the constructing, the conserving and the enhancing orders of things, and with cosmic purpose, whatever that may be—if any there be."

The publishers of this remarkable work make the modest claim that

"every parent will feel that this book . . . is a priceless guide in helping . . . to an understanding of the difficult problems that press for solution every day and every hour." The reviewer feels that the average parent, even with a wet towel about the head and a dictionary at hand, would be unable to wade through the ponderous text, so irritatingly interlarded with capitalizations, italics and asterisks. Certainly one would not recommend that a parent undertake the labor, as the book has nothing to offer but a repetition of vague and muddled generalities.

PATRICIA STEEN.

"Fundamentals in Massage." By KATHRYN L. JENSEN, R. N., General Director of Physical Therapy Instruction to Students in Washington Sanitarium and Hospital School of Nursing, Takoma Park, Maryland, and in Thirty Allied Schools of Nursing. Pages 130. Illustrations 29. The Macmillan Co., New York, 1932.

The book opens with an interesting history of the development of massage, presented in such a manner that it should secure and hold the student's interest. The questions "Do You Know" at the beginning of each chapter, give a definite incentive for reading; and those following each chapter would prove of value to the instructor.

The illustrations are particularly good and greatly assist in understanding how hands and fingers of the manipulator should be placed, and the direction in which pressure should be made.

Since nursing schools are finding that the most effective method of impressing knowledge of the muscular system on the student nurse is by reviewing the position and action of the muscles, while studying massage, the insert on the classification, names, origin, insertion, nerve supply and action of the muscles, together with the graphs of the muscular system, is most commendable.

Throughout the book, the muscles and parts of the body to which definite manipulation may be applied are listed and the movements and purpose is explained in a very understandable manner. Part of Chapter 5 deals with active and passive movements which are so important in the treatment of orthopedic cases. Chapter 7, devoted to the "Massage for Special Ailments," is outstanding; and an important point is the emphasis the author places on the environment and conditions necessary for the best effects.

The descriptive content is well arranged, clear and concise, and contains many practical features, admirably suited to the student mastering massage.

The course as outlined, meets the requirement of the Syllabus of the New York State Education Department, and is therefore not only well adapted for use as a student's text-book, but would also be of invaluable aid to the instructor.

HELEN V. CLUNE.

Prospecting for Heaven. By EDWIN R. EMBREE. 185 pp. New York. The Viking Press.

This book consists of the views of leaders in the social sciences on present-day problems of finance, economics, politics, religion, and physical and mental health insofar as these problems are related to man's present and future welfare. The author arrives at no conclusions and answers none of his own questions. His object is rather to induce the reader to think, and this he succeeds in doing very well. No persons, however materially minded, will read this book without wondering how successfully man and society will deal with the social problems of the present day. While the world has always been faced with acute and pressing problems, when confronted with them now they seem critical indeed.

The book is written in easy conversational style, and much of the thought content, if not the actual words, has been expressed in conversations of leaders in certain fields of thought and endeavor today, including the author, president of the Julius Rosenwald Fund and formerly a director and vice-president of the Rockefeller Foundation; Charles H. Judd, dean of the College of Education of the University of Chicago; Dr. C. M. Hincks of the National Committee for Mental Hygiene; Howard W. Odum, sociologist and author, director of the Institute for Research in Social Sciences of the University of North Carolina; Victor C. Heiser of the Rockefeller Foundation, international sanitarian and director of public health work; and Franz Alexander, psychoanalyst and one of the leading exponents in the United States of the Freudian school of psychology.

The discussions give a review of man's religious, social and material development since the beginning of time. Strangely enough, Dr. C. M. Hincks, whose outlook might be expected to be somewhat pessimistic in that he deals with the prevention of the most serious affliction of man, mental disease, sounded the most enthusiastic and optimistic note of the group. The discussion on psychoanalysis may prove to be too "tough" reading for the non-psychiatrically trained reader. While the book deals with all of the social sciences, the question of mental health and particularly of the need of man's exercising his reason rather than his emotions in solving problems is the author's particular concern.

BROWN.

Pupil Adjustment in the Modern School. By CECILE WHITE FLEMING, Ph. D. Bureau of Publications. Teachers College. Columbia University. New York City. 1931.

This 94-page volume represents the first of a new series in Studies in Education from the Horace Mann School, which is maintained as an integral part of Teachers College of Columbia University. The purpose of the series is to present "sound educational theory" which can be adapted for use in the public schools. The present work concerns the function and accomplishment of a psychological and pupil adjustment service in the Horace Mann School, a progressive development of great interest and undoubted value. The staff of the division of psychological service includes the director, her assistant and a secretary. The director coordinates and integrates the work of the medical and psychiatric services, arranges and supervises special remedial instruction, and carries on the regular program for classification and educational guidance. This program is extremely elaborate, and includes a group mental test for every child at the time of admission, a Stanford-Binet for all pupils in the elementary school and junior high school during their first year in the school, and a Stanford-Binet retest for pupils in grade four and grade five. Throughout each year further information regarding the pupils' mental capabilities and achievements is obtained by group tests and surveys. During the entire school course careful watch is kept on each child's physical condition, personality traits and social adjustment, and the important points are included in the reports sent to the family. Parents then are invited to cooperate in the school's attempt to improve unfavorable habits and characteristics. Frequent conferences between the teachers and the psychological staff, and meetings of the teachers with the parents, contribute to a fuller knowledge and better handling of the children and their problems.

General factors to which consideration must be given in pupil adjustment are listed by the Horace Mann School as follows:

1. Mental quality, or ability to learn.
2. Physical conditions, temporary and permanent; with particular consideration of—
 - a. Nutrition and apparent vigor or energy and
 - b. Physical defects.
3. Ability to read.
4. Quality of present achievement in specific school subjects; achievement previous to current year, if pertinent.

5. Conditions in the home, including
 - a. Economic conditions.
 - b. Social and cultural background.
 - c. Influence of other members of family.
 - d. Conditions for study.
6. Conditions for study in the school, with emphasis upon library facilities.
7. Total program of work, including work in class, extra-class activities in school; activities outside of school, within and without the home.
8. Methods of work in preparing school assignments.
9. Attitude toward school work. Interests. Emotional attitudes.
10. Associates.
11. Personality of teachers and their relations with the particular child under consideration.
12. Ability of teachers to direct study.
13. Character of assignments; activities provided; motivation of work; adaptation of assignments to pupil's ability.
14. Accuracy of grade placement.
15. Suitability of curriculum to needs of pupil.

The author points out however that usually more than one critical element is involved. For example, in the development of feelings of inferiority, many factors, physical defect, gland imbalance, too severe competition in class, nagging by parents, and other causes may all play a part. Undoubtedly the psychological department, with its excellent grasp on the whole subject of pupil adjustment, has removed many causes for failure, and by early treatment of problems checks many incipient breakdowns.

The description of this valuable work as presented by Dr. Flemming is extremely readable and can be recommended to all interested in the education and adjustment of children.

PATRICIA STEEN.

Child Psychology. By BUFORD J. JOHNSON. XII, 439 pages. Price \$4.00. Charles C. Thomas, Springfield, Ill. 1932.

This monograph brings together much of the very interesting observation and experimentation which has been done in recent years in the various institutes for child study and particularly the child institute of the Johns Hopkins University. The material is presented in a clear and understandable fashion. Anyone who is interested in the more recent developments in this field will not go wrong in consulting this book.

LANDIS.

The Quakers as Pioneers in Social Work. By AUGUSTE JORNS. Translated from the German by Thomas K. Brown, Jr. 240 pages. The Macmillan Company, New York, Publishers.

This book was published 20 years ago in Germany. The reason for its publication at this late date in English, is explained by the following statement, "In a period like the present when the upheaval of modern civilization following the Great War, has caused the most vital changes in every field of social and industrial life to take place, the efforts of that sect of Christians called Quakers who have consistently made efforts to follow the injunction of Christ in their conduct and relation to their fellowmen, should be considered."

In the introduction, the author gives a brief outline of the rise of the Quakers in seventeenth century England. The vicissitudes of George Fox, the founder, and of William Penn, his most important disciple in securing a following, are taken up in some detail.

It is interesting to note that from the very beginning the Quakers assumed responsibility for the poor in their own sect. They did this, first by a systematic organization of their charity and secondly by leveling off certain social equalities between classes. It was for this latter reason that they prohibited such "senseless luxuries as frivolous amusements and extravagance in clothing." Furthermore, they endeavored to place those of their own sect who could work in employment and a certain protection was offered these. Because of this practice of placement in industry, they began to realize the necessity of training for various kinds of work. They started a training farm with two objectives, one was to interest people in leaving the cities and going back to the land, and the other was to have them fitted to make a living should they return to the farms. Although this was not maintained over a long period of years, it was quite successful. Similarly, the Quakers organized a colony of spinners at Newlandkirk. This was so well run that in spite of the prevalence of the dole in the seventeenth century, none of these spinners applied for charity over a long period of years.

The author says that the Quakers were the first group in England to emphasize the need of education and equal advantages for both sexes. With this in view, they organized schools. Strangely enough, Latin, because of its judicial use and religious value, was offered in their schools when the great majority of the middle class was illiterate. In Pennsylvania the Quakers went even farther by passing compulsory education laws. There educational advantages were also offered to the slaves.

The Quakers were very active in prison reform perhaps because most of their leaders were incarcerated from time to time, thus they had ample

opportunity to study the abuses in prison procedure and accordingly were very active in endeavoring to abolish them. The abolition of slave trade and slavery was another activity to which they devoted unbounded energy. No Quaker in the United States owned a slave after 1787.

Their contributions to public health were not to be ignored as they supplied various incentives for better education and better medical procedure for physicians. Their work in the care of the insane is well known. They were the first group in England to recognize this as something of a medical problem. The author, though not a Quaker, evidently admires the accomplishments of this sect to no small extent. He feels that at the present time the efforts of the Quakers are devoted more to the strengthening of the world's sense of social responsibility. The Quakers of today consider that one of the chief needs of society is the importance of the conditions under which the great masses perform their daily labor. They do not now demand the leveling off of all class differences, but the mitigation of the feverish intensity of the competition in which the workers are too often sacrificed for profits.

This book will be enjoyed by those who are interested either in something that contributes a bit to the history of social work or to those who would like to know more of the Quakers and their activities.

HESTER B. CRUTCHER.

Psychological Racketeers. By DR. DOROTHY HAZELTINE YATES. Copyrighted 1932. Richard G. Badger, Publisher. \$2.00. The Gorham Press.

Dr. Yates says, "I have written an account that I have tried to make amusing and not too long, and yet sufficiently exact and detailed. And I have been careful to preserve the delicious expressions of the 'Applied Psychologists'!"

In the opening pages we are introduced to the "applied psychologist," whose flamboyant poster may even outdo the late P. T. Barnum in his most halcyon days, (The reviewer has already caught the spirit of the use of superlatives.)

The earliest chapters tell us the why and how the author developed her examination into this expose of "fakers" and "fakirs." In a lively, almost conversational style, she shows us the beginning of the investigation. How she and her students became more and more intrigued and finally surrendered to the positive mania for "taking in" lectures and being "taken

in" by lecturers. Quotations from the "patter," the claims and the pseudo-scientific "blah" are accurately set down, all evidence gathered is correct in detail, but actual names have been omitted except in one celebrated case where she has compiled, from many sources, a record of one individual whose activities became positively criminal.

While reading the text one is highly entertained by the statements of the impostors but one also becomes pathetically sympathetic with Barnum's fools who are so thoroughly misled by this buncombe "ology," which can read your mind, change your life completely, make your dreams come true, etc., etc.

In referring to one "Professor" she states: "—It is the only evidence I have been able to obtain that any of the 14 "applied psychologists" have made any attempt at a special study of psychology at a university of standing." When you consider this fact and then look at the type of men and women whom she represents as engaged in this racket you are struck with the amount of shrewdness they possess and the pure and unadulterated native talent they have for understanding human nature.

Chapter headings give us a good insight into the context. In the first we meet an amusing character who calls upon the cooperation of the body to assist the psyche to restore the client. Chapter three tells us, "how they put it over;" and Chapter four, at "what price psychology." The next two show what is taught, tables being included with data on the subjects most frequently met with in their circulars. A chapter on "Qualifications, Education and Credentials" discovers a surprising lack of any real foundation, unless one is "taken in" by the fine sounding and sonorous titles, like D. O. and C. P. degrees. Several discuss the various "systems" and how they are marketed. The penultimate opens with "Humpty Dumpty said the way to tell anything was to begin at the beginning, go through to the end, and then stop." But the rule will not do for the "applied psychologists," for woman-like she must have the last word, "Before we part company, let us consider together what trained psychologists think about some of the less wildly extravagant concepts of "applied psychology." The concluding chapter is her own contribution and is worth the price of the book.

There are some typographical lapses but they may be excused, as likely to occur in any work where so many superlatives are quoted. One can easily read the book in an evening but will find himself later often recurring to the final chapter.

GRAY.

Emergency Work Relief. By JOANNA C. COLCORD, WILLIAM C. KOPLOVITZ and RUSSELL H. KURTZ. 279 pages. Russell Sage Foundation, 1932. Cloth, \$1.50.

The experiences of 26 American communities during the winter of 1930-31 with administering relief, come at a most opportune time, and the suggestions for setting up such programs in other communities are valuable. In this book programs financed entirely by public funds, entirely by private funds and by both sources were studied, under the following heads; inception of program, method of administration including personnel, registration and investigation, assignment of wages, and methods of controlling these so that needed relief would be given in proper places. Mention is also made of relief given without work or wages. The extent of work, its cost in administration, total wages given, etc., are covered in the study of each city. The location of the cities studied is somewhat limited geographically, chiefly in the middle, eastern and southern states, but the cities vary as to size, type of population, type of industries, etc., so that one feels that a fair sampling of work done for relief meeting various types of situations throughout the United States is well depicted. The third part of the book is devoted to suggestions for setting up a work relief program, its underlying concepts, its planning, personnel, office system, etc. While this book is primarily for those administering emergency work relief, it should be more widely read so that the difficulties of such a program and its extent in various places might be better understood.

HESTER B. CRUTCHER.

Principles of Mental Development. By RAYMOND H. WHEELER, Ph. D., and F. THEODORE PERKINS, Ph. D. XXIV + 529 pages. Price \$3.75. Thomas Y. Crowell Company, New York, 1932.

This is an advanced and comprehensive text of educational psychology. It has been written from the organismic or Gestalt standpoint. The material is treated in a rather conventional way with the point of view of the authors added in the manner of a sauce or seasoning. Much of recent experimental findings have been incorporated in the text. It should be of interest to the physician who is following the more recent developments in educational fact and theory.

LANDIS.

Psychology Today. Edited by Walter V. Bingham. XII + 271 + 44 + 48 + 32 + 32 + 32 + 36. \$1.50. University of Chicago Press, 1932.

During the winter of 1931-1932 the National Advisory Council in Radio and Education sponsored a series of 30 weekly talks on present-day psychology. These addresses were given over a nation-wide network of the National Broadcasting Company. The talks, as delivered, have been assembled, together with the study manuals which accompanied each of the series and the collection has been brought out by the University of Chicago in the present volume. The general topics covered were: Psychology today, child development, our changing personalities, animal behavior, psychology and education, and psychology in industry. In each case an effort was made to have speakers who had been working in the particular field speak upon the topics assigned. The five addresses on "Our Changing Personalities" were entitled, "Transient Changes in Personality," by F. A. Moss; "How to Grow a Personality," by J. B. Watson; "Growing Older," by C. Landis; "Personality in Our Changing Society," by F. H. Allport, and "Mending Broken Personalities," by F. A. Moss. Each of these talks was given from the mental hygiene standpoint. This collection of essays represents a popular, readable summary of the field of present-day psychology. Much of the material is well known to professional psychologists but probably the most of it was new to the popular audience.

LANDIS.

Studies in the Dynamics of Behavior. By P. STONE, W. DARROW, C. LANDIS and L. L. HEATH. (Edited by K. S. Lashley.) XIV + 332. \$5.00. University of Chicago Press, Chicago, 1932.

In 1927, The Social Science Research Council made available to the Behavior Research Fund a grant for the study of emotional factors which might contribute to the delinquency of children. The present book is a report of three of the investigations made possible by this grant. Stone investigated wildness and savageness in different strains of rats. He showed that there is a constant difference in the behavior of a wild or savage rat and that of the untamed albino rat. The differences are persistent and are probably due to hereditary rather than environmental factors. He further showed that the wildness did not necessarily effect the learning ability of the animal if proper handling and motivation were employed.

Darrow made use of the Thurstone Neurotic Inventory, the Northwestern

Introversion-Extroversion test together with various physiological measurements upon four groups of individuals. Three of these groups were University freshmen who made extreme scores on the neurotic inventory, while the fourth group was made up of individuals who were markedly extroverted on the basis of the Northwestern test. These groups were analyzed physiologically by measurements of the galvanic skin reflex, blood pressure and respiratory activity. He found no relationship between the scores which these students made upon the tests and their physiological reactions.

Landis gave tests of personality, temperament, ascendancy-submission, humor, emotionality, learning, intelligence, suggestibility, school progress and measurements of the galvanic skin reflex to a group of 100 delinquent boys in the Chicago Detention Home, and to 125 girls, at the Connecticut Long Lane Farm. He found that neither age, race nor social offense was related in any constant fashion to either emotional stability or to any of the tests which he used. An analysis of the individual test performances with respect to conformity or non-conformity of each individual as compared to the entire group, showed that conformity with respect to the test employed did not agree with conformity in general life-situations. In general, it was concluded that analytical investigations of the personality traits of emotionality or psychopathy are unsatisfactory and fail to bring out decisive diagnostic evidence.

LANDIS.

Prohibition and Mental Hygiene. Article by FREDERICK W. BROWN. In the *Annals of the American Academy of Political and Social Science*, for September, 1932.

Knowledge concerning the effect of alcohol upon mental health was sought through a study of the statistics of admissions to mental hospitals and to general hospitals. Specific reference is made to the relation of alcohol to mental deficiency, epilepsy and mental disease. The principal sources of data are: the statistical reports of the New York State Department of Mental Hygiene and the United States Bureau of the Census; and questionnaires returned by the superintendents of hospitals for mental diseases, institutions for mental defectives and epileptics and general hospitals.

MENTAL DEFICIENCY

Opinions with respect to the interrelations of alcohol and mental deficiency are contradictory, and range from definite statements of a causative association to the skeptical conclusion that the available evidence does not

yet justify any opinion. Statistics with respect to first admissions to 30 State institutions for mental defectives in 1931 indicate that of 4,019 cases, 3,778, or 94.0 per cent, showed no history of alcoholism in any form. In the remaining 6.0 per cent, an alcoholic heredity was present, or the patient was admitted because of conduct resulting from excessive use of alcohol, or the patient was admitted because of parental neglect resulting from excessive use of alcohol. (It should be noted, however, that there are no comparable statistics for the general population.)

EPILEPSY

The same inconclusiveness in opinion and in statistics exists with respect to epilepsy. A study of 1,084 new admissions to 14 State institutions for epileptics in 1931 showed that 986, or 91.0 per cent, had no history of excessive use of alcohol; in 65 cases, or 6.0 per cent, alcoholic heredity was strongly indicated, and in 33 cases, or 3.0 per cent, the patient was admitted because of conduct resulting from excessive use of alcohol.

ALCOHOLIC PSYCHOSES

Earlier studies showed that an alcoholic psychosis resulted from alcoholic indulgence over a long period of years, the average period among admissions to the New York civil State hospitals being 22 years for men, and 16 years for women. A previous study by Pollock and Brown showed that males exceed females in the alcohol psychoses by a ratio of from 4 to 7.5:1; three-fourths of the admissions in this group are between the ages of 30 and 55; they are predominantly from an urban environment; and the economic condition of the great majority is marginal.

In recent years the following changes have been noted in the type of patient suffering from alcoholic psychoses. General hospitals report serious complications as a result of the poisonous nature of the beverages consumed. State hospitals report fewer cases of prolonged or chronic hallucinosis, and more cases of alcoholic poisoning. State hospitals also report an unusually large group of young patients.

GENERAL HOSPITAL STATISTICS

Twenty-nine hospitals reported a total of 242,347 patients treated during 1931. Of these 838, or 0.4 per cent were cases of alcoholic psychoses; 9,614, or 4.0 per cent, were cases of alcoholism without psychosis; and 1,198, or 0.5 per cent, were cases in which alcohol was an important complicating factor. Reports from 8 general hospitals relative to their psychopathic departments only, showed that of 9,534 patients received in 1931, 383, or

4.0 per cent were cases of alcoholic psychoses; 2,029, or 21.3 per cent, were cases of alcoholism without psychosis; and 136, or 1.4 per cent, were cases in which alcohol was a complicating factor.

STATE HOSPITAL STATISTICS

Of 52,155 first admissions to all hospitals for mental disease in the United States in 1922, 1,819, or 3.5 per cent were cases of alcoholic psychoses; of the 11,248 readmissions, 355, or 3.2 per cent, were alcoholic psychotics. Among 228,399 resident patients on January 1, 1923, 6,430, or 2.8 per cent, were alcoholics. Of the 59,417 first admissions to State hospitals for mental disease in 1928, 2,770 or 4.7 per cent were cases of alcoholic psychoses; and 1,126, or 1.9 per cent, were cases of alcoholism without psychosis. Of the 13,971 readmissions, 535, or 3.8 per cent, were alcoholics, and 266, or 1.9 per cent, were alcoholics without psychosis.

Statistics of first admissions to the New York civil State Hospitals, show that new cases of alcoholic psychoses represented a declining percentage of all admissions from 1909 to 1915. After an increase between 1915 and 1917, the percentage fell again until 1920. From the latter year to 1927 the trend rose steadily. The same general picture is shown by the statistics of intemperate users of alcohol admitted to these hospitals. Similar statistics for other states show that 1920 marked a turning point. Prior to this year, there was a declining trend in the rate of admissions with alcoholic psychoses; since 1920 there has been a rising trend. Deaths from alcoholism have also shown a rising trend since 1920. There appears to be a marked correlation between the prevalence of alcoholic psychoses and the percentages of foreign-born and urban populations.

MALZBERG.

Alcohol and Man. The Effects of Alcohol on Man in Health and Disease.

Edited by HAVEN EMERSON, M. D. Pp. vii, 451. \$3.50. The Macmillan Co., 1932.

The word alcohol is shot through with so much emotional content and the whole subject is beclouded with so much mis-information and lack of information that the word *timely* is the most obvious characterization of "Alcohol and Man." Its authoritativeness is vouchsafed by the imposing names in the list of editors and contributors. Holding closely to the strict scientific approach, and written for the intelligent layman, it should go far to make clear to ardent drys and wets what re-statements of their claims and counterclaims must be made if the impartial verdict of very extensive

scientific investigations is to be made arbiter of the truth. The title page of the book might have borne the motto of Dunoyer, "Je ne propose rien, je ne même dispose rien, j'expose."

At all points the authors try to avoid propaganda and let facts speak for themselves. Perhaps the nearest to transcending this principle on the dry side is the very clever sketch on page 136. The sketch, in comic strip style, carries the hero through the stages of various concentrations of alcohol per cubic centimeter of blood, "Less than 1 milligram, Dry and Decent; 1-2 mg., Delighted and Devilish; 2-3 mg., Delinquent and Disgusting; 3-4 mg., Dizzy and Delirious; 4-5 mg., Dazed and Dejected; more than 5 mg., Dead Drunk." And on the wet side the instance would be the contribution beginning page 161 which gives a verdict in favor of the use of alcohol in old age but without any reading references either as footnotes or at the end of the chapter, without any survey of the literature or the historical development of the position taken or any reference to statistical, experimental, or clinical records. This manner of treatment is quite in contrast with most of the articles, which are carefully documented and state the experimental or other basis for the conclusions reached.

The "intelligent layman" for whom the book is written will learn that in scientific circles there is no question concerning the classification of alcohol as a narcotic and depressant whose erstwhile reputation as a stimulant is due to its power to bring about an "inhibition of inhibitions." The Freudian equivalent of this, in terms of the ego and the id, is given on page 73. The significance of lengthened reaction time and of impaired co-ordination of muscles in an age of machinery and automobiles is hinted at but without argument.

The trend away from the free use of alcohol as a therapeutic agent in the best hospitals and among private practitioners is developed with detailed references.

One of the findings that will surprise the average layman is the relative clean bill of health that can be given to bootleg liquor on the ground, first, that the distinctively harmful agent is ethyl alcohol itself, and, second, that the common practice of dilution in the interest of greater profits reduces the effect as compared with higher grade beverages.

One of the striking charts is that on page 356 showing the rapid decline in the rate of admission to New York civil State hospitals on the part of patients suffering from alcoholic psychoses during the years 1909 to 1920, followed by a period of increase from 1920 to 1931, though not up to the earlier level. "Alcohol is a direct and principal cause of several types of mental disease." "The low rates of alcoholic mental disease and other so-

cial gains in New York and Massachusetts in 1920 indicate the possibility of eliminating most of the evils arising from excessive use of alcohol."

As the chapters are written by different authors certain consistencies appear, e. g.: On page 30 we read, "The odor of the breath after alcoholic drinks is due to constituents other than alcohol," and on page 138, "The odor of ethyl alcohol is so distinctive that most people can readily identify it on the breath of a person who has recently indulged. The odor of alcohol is not in itself sufficient to make a diagnosis of intoxication, since a small quantity of alcohol, far too small to have physiological effects which would justify a diagnosis of drunkenness, might still be amply sufficient to cause a recognizable odor around the mouth and on the breath of the subject."

"Alcohol and Man" deserves wide attention. The extent to which it is used will be significant concerning the extent to which society is willing and able to be guided in scientific thinking concerning a matter of great concern.

It is much to be desired that a companion volume bringing information up to date on the economic, fiscal, and legal aspects of the liquor problem might in like manner be prepared by a board of experts.

S. W. WILCOX.

How to Develop Your Personality. By SADIE MYERS SHELLLOW, Ph. D.
308 pages. 1932. Harper & Brothers, New York.

Procuring mental health and the contribution which mental hygiene has to make toward the efficiency and happiness of the normal individual have been stressed for the last 20 years. The actual techniques of making the changes in habits and attitudes for the improvement of one's mental health have probably never before been as comprehensively assembled and as interestingly put forth for the lay person. Dr. Shellow attempts to define personality and to tell how it is judged; to tell how to evaluate one's own assets and liabilities on various levels; how to supplant undesirable habits with desirable ones; what constitutes social adaptation with suggestions as to its development.

In the text are given tests of general trends and abilities which almost anyone would find interesting to take. Illustrative material is chosen from every-day experience which gives one an understanding and a humorous appreciation of the universality of foibles. At the same time the book is inspiring so that the reader is "sold" to the idea of developing his own personality.

This book can be safely recommended to the lay person interested in self-improvement and the probabilities are that whoever starts the book will read it with avidity.

HESTER B. CRUTCHER.

Medical Care for the American People. Final Report of the Committee on the Costs of Medical Care. 223 pages. Price \$1.50. The University of Chicago Press, Chicago, Illinois. Baker & Taylor Company, New York.

This is an exceptionally satisfactory book. It deals with a social subject of great importance; it is the outcome of careful study and research; it is written in a direct, forceful style and conveys a comprehensive message in few words; it sets forth a workable plan to promote a professional undertaking for the benefit of the American people; and gives lucid arguments for and against the plan. No one can read the book without being impressed with the skill and ability manifested by the executives of the Committee on Costs of Medical Care in pursuing their purpose.

In the opening chapter the present status of medical care in the United States is discussed. Statistics are given relative to the personnel engaged in providing medical care to the patients in hospitals of different kinds in the United States, and the medical services needed and received. After a thorough-going analysis of the data the committee concludes that the people need a substantially larger volume of scientific medical service than they now utilize; that modern public health services need to be extended to a far greater percentage of the people; that there is need for a geographical distribution of practitioners and agencies which more closely approximates the medical requirements of the people; that in rural and semi-rural areas the current expenditures for medical care are insufficient to insure adequate services; that there should be an opportunity for many practitioners to earn larger net incomes than they now receive; that there should be better control over the quality of medical service provided; that there is need of reduction of waste in many different directions and that the prevailing methods of purchasing medical care have unsatisfactory consequences.

In the second chapter the essentials of a satisfactory medical program are outlined. In brief the plan provides for safeguarding quality of medical service and personal relations, for meeting the people's real needs, for service on acceptable terms, for emphasis on preventive measures, for selection of competent practitioners and for adequate payment to practitioners and agencies. After a discussion of these points, the committee reaches the conclusion that the plan can be best realized by a system of group practice. Much of the remainder of the work deals with the problems of the organization and adjustment of such group practice to the needs of the public and to the interests of practitioners. It is suggested that the physicians constituting a group unit should receive definite salaries which would be paid by an insurance plan whereby all families engaging the services of

the group would pay a stated amount month by month and would be entitled to receive from the group such medical service as the members of the family might need. In some of the poorer sections a certain amount of State aid would be necessary.

The report of the majority of the committee did not receive the approval of all of the members. A minority group of nine voiced a decided objection against State medicine and against corporate boards of medicine and recommends that united attempts be made to restore the general practitioner to the central place in medical practice. The views of this group are said to represent in large measure the views of the executives of the American Medical Association.

Two dental members of the committee, while agreeing with the recommendations of the majority with reference to group practice, feel that certain features of the majority plan are not workable.

An interesting opinion is written by Walton H. Hamilton and a note explaining reasons for not signing the report by Edgar Sydenstricker.

The final report of the committee has attracted wide attention and it seems probable that attempts will be made in many parts of the country to put the committee's recommendations into effect.

POLLOCK.

A Standard Classified Nomenclature of Disease. Compiled by the National Conference on Nomenclature of Disease, and edited by H. B. Logie, M. D. C. M. The Commonwealth Fund, New York.

Long before this new nomenclature was undertaken it had been recognized that the classification of disease was not on a satisfactory basis. It is true that an international list of diseases had existed since 1855 and had undergone several modifications, but no one claimed that the list constituted an adequate or truly scientific classification of disease. It had not been prepared in accordance with fundamental principles of classification and had not kept pace with the progress of medicine in the various specialities. Several other classifications of disease had been devised and used to a greater or less extent but none of these had gained general approval.

With a view to the preparation of a more scientific and complete classification of diseases a group of physicians connected with the New York Academy of Medicine and backed by the Commonwealth Fund started, in 1928, an organization which became known as the National Conference on Nomenclature of Disease. The membership of the conference consisted of 27 medical and administrative organizations such as the American Dermatological Association, the American Gynecological Society, the American Heart Asso-

ciation, the American Hospital Association, the American Orthopedic Association, the American Psychiatric Association, the American Medical Association, the American Statistical Association, the American Surgical Association, the U. S. Army, the U. S. Bureau of Census, the U. S. Veterans' Bureau, etc. Each organization was permitted to send one or more delegates to the meetings of the conference. Dr. Haven Emerson was made president of the conference, Dr. George Baehr, secretary, and Dr. H. B. Logie, executive secretary. The formulation of the new classification is largely the work of Dr. Logie. He has, of course, been assisted by representatives of all the medical specialties.

At the outset it was decided that two principles of classification should be used, namely; the organ affected or the site of the disease, and the etiology or cause of the disease. Each specific disease was to carry a code number that would clearly indicate both factors to one familiar with the system. To secure this result it was necessary to establish primary, secondary and tertiary categories of body organs and likewise primary, secondary and tertiary categories of causes. As a decimal system of code numbers was to be used, the general categories of organs were limited to 10. Likewise, 10 principal divisions were made of the general causes of disease.

A code number accordingly consists of two divisions each of three digits, the two divisions being separated by a dash; for example, tuberculous of lung would be designated by the code number 360-123. The first part, 360, indicates the site of the disease, and the second part, 123, the cause. The digit 3 in the first part represents the respiratory system, the digit 6, the lung, and the digit 0 indicates that the organ as a whole is affected. In the second part of the code number, the digit 1 indicates that the disease is due to infection, and the digits 2 and 3, that the germ causing the disease is the bacillus tuberculosis. In like manner syphilis of the lung would be designated by the code number 360-147; the second number, 147, representing syphilis, wherever used.

As the system of classification has been developed with remarkable understanding and skill, the finished work marks a new epoch in the scientific classification of disease.

Through the cooperation of representatives of the American Psychiatric Association, and the New York State Department of Mental Hygiene, the present classification of mental disease and that of convulsive disorders were incorporated into the general nomenclature in satisfactory manner. Through the aid of representatives of the American Association for the Study of the Feeble-minded a new classification of mental deficiencies was also made available.

The new nomenclature should prove of great service in the advancement of medical science and in the statistical reporting of morbidity and mortality.

POLLOCK.

The Wholesome Personality. A Contribution to Mental Hygiene. By WILLIAM H. BURNHAM, Ph. D. 713 pages. D. Appleton and Company, New York and London.

The scientific method, which consists so largely of analysis, requires that any given problem be separated into parts as elementary and distinct as possible, in order that each part may be studied under specified conditions. Applied to the physical sciences and even to certain aspects of the biological sciences, this method has broadened our knowledge immeasurably. When applied to the study of the behavior of human beings, however, the method is subject to error arising from the fact that we cannot build up the whole merely from a knowledge, however complete, of its parts. The whole is itself an entity in the manner made so clear by the exponents of the *gestalt* psychology. It is the uniqueness of this whole, which we sum up in the concept of personality, and the maintenance of personality in a healthy or wholesome balance, which form the subject matter of this encyclopedic volume of 700 pages.

The central element in the survey of the wholesome personality is the fact of integration. Evidence is brought forth to prove that the rich and successful personality is the one in which the parts are organized and adapted to each other so as to work as a harmonious unit. It is the function of the mental hygienist to understand the processes of integration, and, contrariwise to discover the conditions which result in disintegration. In surveying these two aspects or conditions of personality, Professor Burnham gives us a complete story of mental hygiene, and its relation to such varied disciplines as general medicine, physiology, psychology, anthropology and sociology. The nature of personality, the manner of its growth, and its intimate dependence upon a variety of conditions clearly justify the detailed excursions into so many branches of science.

In the difficult period through which the world is passing, there are many stimuli to a disintegration of personality. Fears, mental complexes, and emotional disturbances are assailing multitudes of people. At such a time therefore it is a source of gratification to be able to find a book as satisfactory and sensible as that which Professor Burnham has provided us with. It should help many troubled individuals to maintain that integration which is the sign of the wholesome personality.

MALZBERG.

Problems in Human Engineering. By F. ALEXANDER MAGOUN, S. M.
535 pages. Price \$3.50. The Macmillan Company, New York.

Professor Magoun presents here 50 problems which were submitted to the class in humanics at the Massachusetts Institute of Technology. Perhaps that suggests the reason for using the word "engineering" in the title of a book dealing with broad problems of human relationships and practical applications of psychology, which are by no means limited to those engaged in the profession of engineering.

The problems are of such a nature that there is no one best answer to any of them. There are too many imponderable factors, diverse personalities, complex situations, predicaments involved to make one set answer possible. But answers can probably be classed as satisfactory or unsatisfactory, adequate or inadequate, possible or impossible, relevant or irrelevant, responsive or unresponsive. Following each problem is a group of answers submitted by students, each of which answers might be designated by one or more of the terms suggested. The book therefore is really a symposium of the students' reactions to and solutions of the problems presented. It represents an effort to encourage the individual to think for himself—a phenomenon altogether too infrequent, and the results given show a range from clearly inadequate to very satisfactory. It can not be said, however, that the answers generally suggest the immaturity of youth, as one might expect. On the other hand, they come from a carefully selected group of persons of presumably superior intelligence and a maturity of thought above the general average.

The author in his introduction truly says that "maturity is not a question of years, nor even of experience, but rather the result of an intellectual and spiritual development which comes only with the wise solution of one's difficulties * * * Surface maturity may be a mere matter of conventions and manners, but fundamental maturity is based on an understanding of human relationships"—a statement in accord with the concepts of mental hygiene.

Here is a sample problem: Since graduation 15 years ago, you have worked for one company, almost half the time as assistant superintendent. The superintendent has been a second father doing everything possible to give you experience and instruction. Two years ago he had a stroke from which he has improved only enough to come to the office a few times a month; but he still draws his salary. You gladly took over his duties and responsibilities, but you have had both now two years, without the rank and remuneration, and you resent it. There are conflicting loyalties. After seriously considering your duties to the company, the superintendent, your family, and yourself, decide what to do.

The book should be helpful to teachers and students of college grade, and of interest to those general readers who like thought-provoking, imagination-stimulating reading, having to do with human relationships. To such it is recommended.

FARRINGTON.

Man and Medicine. An introduction to medical knowledge by DR. HENRY E. SIGERIST with an introduction by Dr. William H. Welch. Pp. X-340. Price \$4.00. W. W. Norton and Company, 70 Fifth Avenue, New York City.

Dr. Welch in his introduction praises Dr. Sigerist's book as one that is unique in bringing together a picture of modern medicine with its historical and cultural background. He says: "I know of no other work covering in its entirety the same broad field, certainly none combining in equal degree complete command of the history of medicine with full knowledge of the present state of the science and art of medicine and with penetrating insight into the past and present social, cultural and philosophical bearings of the doctrines and practices of the healing art."

The above is a terse characterization of Professor Sigerist's unusual book. It is made up of seven divisions dealing first with anatomy and physiology, not in text-book style but as a philosophical consideration of important discoveries and events with descriptive pictures of the historical backgrounds and the intellectual development of the times and of the men who accomplished great things in medical science. He links it also with the art and literature of the epoch and presents sometimes with detail, the scene upon which developed the important events which marked the progress of medicine. Passing on to diseases, the early and later conceptions of disease, the general theory of diseases, he treats of these in the same comprehensive manner. Later chapters are devoted to the external and internal causes of disease, to diagnosis, prophylaxis, and the sphere of the physician. He advises the students to try to understand not alone diseases but the man himself who comes to them. In the university they studied psychology, philosophy and sociology to round out the picture of man which the physician must possess, and proceeds: "Observation and reflection are the most vital attributes of the medical practitioner. But we must not confine our observing and meditating to that which is pathological. It must take in all that goes on about us. How much we may learn on our daily walk through the streets! What fateful stories we may gather from a few snatches of dialogue, what pictures of life we may get in a glance through an open doorway! Traveling through the open country we will ponder over the

difference between life in town and country, meditate on the influence of environment upon the rhythm and cycle of man's existence."

It is an interesting book based upon lectures to medical students whose outlook upon their chosen profession must have been vastly broadened by hearing them. It can be understood by educated people generally and will be equally instructive and interesting to them also. The translation by Margaret Galt Boise has well preserved the author's smooth and clear literary style.

Professor Sigerist is the professor of History of Medicine and director of the Institute of Medical History at the University of Leipzig. He was in this country last year as visiting lecturer at the Johns Hopkins University.

HUTCHINGS.

DR. DAVID CORCORAN BECOMES SUPERINTENDENT OF CENTRAL ISLIP STATE HOSPITAL

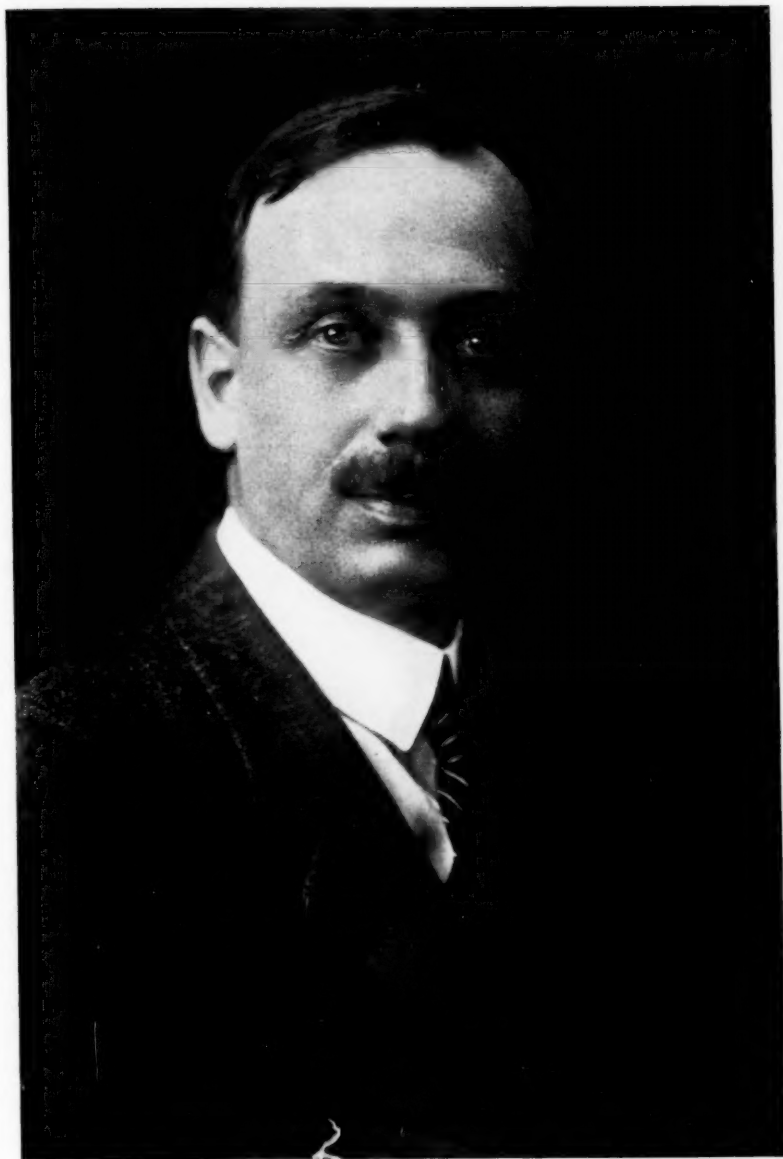
Dr. David Corcoran, who had been first assistant physician at the Creedmoor division of the Brooklyn State Hospital since 1925, was appointed by Commissioner Frederick W. Parsons superintendent of Central Islip State Hospital, January 1, 1933. He succeeds Dr. George A. Smith who retired December 1, 1932.

Dr. Corcoran was born at Crawford, Orange County, N. Y., July 16, 1881. His preliminary education was received at Montgomery Academy, Montgomery, N. Y., and at Middletown High School, Middletown, N. Y. He entered the College of Physicians and Surgeons of Columbia University in 1901 and graduated in 1905. He served a medical and surgical internship at St. Vincent's Hospital, New York City, from 1905 to 1907. He entered the New York State hospital service as a junior assistant physician in Central Islip State Hospital in September, 1907. He was promoted to assistant physician in 1909, to senior assistant physician in 1911, and to clinical director at the Brooklyn State Hospital in 1918. He was transferred to the Creedmoor division as first assistant physician in 1925. His administration of this new hospital during its development period demonstrated his marked ability as a hospital executive.

In 1915, Dr. Corcoran took a special course in training in the Psychiatric Institute. He has manifested a broad interest in psychiatry and has presented several papers at quarterly and interhospital conferences.

Dr. Corcoran is a member of the following societies: Medical Society of the County of Kings, New York State Medical Society, American Medical Association, American Psychiatric Association, New York Society of Clinical Psychiatry, New York Society of Medical Jurisprudence, Brooklyn Neurological Society and Associated Physicians of Long Island.

Dr. Corcoran married Julia Frances Begley in June, 1913. He has three sons, David Begley, 17; John William, 14, and James, 13. His wife died in October, 1923.



DAVID CORCORAN, M. D.





CHARLES S. PARKER, M. D.



DR. CHARLES S. PARKER IS PROMOTED TO THE SUPERINTENDENCY OF KINGS PARK STATE HOSPITAL

Dr. Charles S. Parker, who had been first assistant physician at the Kings Park State Hospital since December 22, 1922, and acting superintendent since November 16, 1931, was appointed by Commissioner Frederick W. Parsons superintendent of the hospital, January 1, 1933. He succeeds Dr. William J. Tiffany who was transferred to the superintendency of Pilgrim State Hospital.

Dr. Parker was born at Three Mile Bay, March 10, 1887. After graduation from the high school of his native village he entered the Medical School of Syracuse University in 1904, and received the degree of Doctor of Medicine therefrom in 1909. He began hospital work as an interne in Mercy Hospital, Wilkesbarre, Pa., in June, 1909, and continued in such position until his appointment as medical interne in Kings Park State Hospital, October 1, 1910. He was promoted to junior assistant physician, February 1, 1911; to assistant physician, April 1, 1911; to senior assistant physician, June 22, 1918; and to first assistant physician, December 22, 1922. At the time of Superintendent Tiffany's transfer, Dr. Parker became acting superintendent of the hospital. His promotion to superintendent is fitting recognition of his successful management of the institution during the past year.

Dr. Parker is a member of the American Psychiatric Association, Suffolk County Medical Society, New York State Medical Society, and Long Island Psychiatric Society.

Dr. Parker married Elizabeth MacConnell of Brooklyn, N. Y., on May 17, 1916. They have two children, Charles William, 14; and Jean Elizabeth, 12.

DEATH OF DR. GEORGE M. KLINE

Dr. George M. Kline, commissioner of the department of mental diseases of the State of Massachusetts, and internationally-known psychiatrist, died of heart disease at his home in Boston, January 5, 1933.

Dr. Kline was born in Pittsburg, Pa., March 6, 1878. His preliminary training was received in the public schools of Grand Rapids, Mich., and his medical education in the University of Michigan. Following graduation in 1901 he became assistant physician in the Worcester (Mass.) State Hospital. After serving a year in such position he accepted an appointment in the Mount Pleasant (Iowa) State Hospital where he continued until 1906. He then became a member of the staff of the State Psychopathic Hospital at Ann Arbor, Mich. Six years later he was appointed superintendent of the Danvers (Mass.) State Hospital. In 1917, he became commissioner of the department of mental diseases of Massachusetts. His long service in this responsible position was marked by well-devised progressive steps.

For many years Dr. Kline was a leader in the work of the American Psychiatric Association and was its president in 1927. He was active in the work of the National Committee for Mental Hygiene, and the Massachusetts Society for Mental Hygiene, and was a member of the Medical Council of the U. S. Veterans' Administration. He received from the republic of France the decoration of Chevalier of the Legion of Honor.

The esteem in which Dr. Kline was held by all who knew him was well expressed by former Governor Frank G. Allen when he said:

"Dr. George M. Kline was an outstanding specialist in his field. His opinion and views upon the treatment of the insane were sought by authorities not only in North America but in Europe. He had thus become an international authority. For nearly 15 years Dr. Kline made the institutions for the insane in Massachusetts his first interest. He brought them up to the highest point of efficiency in the history of the state. In his death, Massachusetts loses one of its ablest administrative heads."

After learning of Dr. Kline's death on January 6, Dr. Frederick W. Parsons, New York State Commissioner of Mental Hygiene, sent the following telegram to the Department of Mental Diseases in Massachusetts:

"New York State joins with Massachusetts in deploring Dr. Kline's death. His was a record of outstanding achievement in the mental hygiene field and his leadership will be missed in the councils of his associates."

NOTES

Dr. S. Spafford Ackerly has been appointed director of the Louisville Psychological Clinic.

—Dr. Edward Nathaniel Brush, dean of American psychiatrists, died of pneumonia at his home at Mount Washington, Baltimore, January 10, 1933.

—The tenth annual meeting of the American Orthopsychiatric Association will be held at the Hotel Pennsylvania, New York City, February 23, 24, 25, 1933.

—Dr. Herbert E. Chamberlain, former director of the Child Guidance Clinic of the Board of Education of Minneapolis, has been appointed associate professor of psychiatry in the University of Chicago.

—Dr. Frederick W. Parsons was reappointed by Governor Herbert H. Lehman on January 5, 1933, to the position of State Commissioner of Mental Hygiene. The Senate immediately confirmed the appointment. Dr. Parsons was originally appointed by Governor Smith in 1927.

—Dr. M. A. Bliss of St. Louis, a pioneer worker in mental hygiene, was signally honored by the State of Missouri for his contributions in this field. A medal was conferred on him on June 24, 1932, by the governor of Missouri "for distinguished service in mental hygiene in Missouri."

—Dr. James V. May, superintendent of Boston State Hospital, and former New York State Hospital commissioner, has been appointed commissioner of mental diseases for the Commonwealth of Massachusetts. He succeeds Dr. George M. Kline, who died January 5, 1933.

—The Children's Bureau of the U. S. Department of Labor, in a recent bulletin states that juvenile delinquency cases in children's courts showed an upward trend from 1927 to 1930. There was a drop of 8 per cent in 1931, but the decrease was principally in the less serious offenses, such as truancy and being uncontrollable. Stealing cases continued to increase.

—The New York State Crime Commission has issued its final report, which consists in an analysis of youthful offenders between the ages of 16 and 21. The report points out the numerical importance of this group, and urges the creation of special courts, equipped with adequate psychiatric and psychologic services, and probation staffs, to meet their needs.

—The Council of the American Psychiatric Association announces that the next annual meeting of the Association will be held at the Hotel Statler, Boston, Mass., May 29-June 2, 1933. The president of the Association for the current year is Dr. James V. May and the secretary, Dr. Clarence O. Cheney.

—Dr. Horatio Gibson, former first assistant physician of the Central Islip State Hospital, died at his residence in Douglaston, N. Y., December 13, 1932, at the age of 67. His death was due to cerebral hemorrhage.

Dr. Gibson was the son of Brig. General Horatio G. Gibson. He entered the State hospital service in 1896 as junior assistant physician at Manhattan State Hospital. In 1901, he was transferred to Central Islip State Hospital where he served until his retirement on July 1, 1931.

—Dr. William Sydney Thayer, former president of the American Medical Association, distinguished clinician and teacher of medicine, died in Washington, D. C., of heart disease, December 10, 1932, at the age of 68. In addition to his work as a medical practitioner and professor, Dr. Thayer carried on extensive researches and published many important monographs. His contributions received world-wide attention and he was given many honors by foreign universities.

—The Commission on Medical Education of which Dr. A. Lawrence Lowell is chairman, has issued a report prepared for the Association of Medical Colleges. The report finds that there are at least 25,000 physicians too many in the United States; that specialization is being carried to excess, that pre-medical education should be stressed in secondary schools in order that the period of education may be shortened. Sickness insurance is said not to be a cure-all for the economic problems involved in medical care.

—The Division of Psychiatric Education of the National Committee for Mental Hygiene has completed the first year of activity, and reports substantial progress. Many of the medical schools have asked for advice concerning the teaching of psychiatry and several have increased their facilities for training in psychiatry. Several hospitals for mental disease are providing greater opportunity for the training of internes in psychiatry. Yale University Medical School is cooperating with the New Haven Hospital in a demonstration of the value of clinical data in general hospitals as teaching material in psychiatry.

—The Statistical Bulletin of the Metropolitan Life Insurance Company for September, 1932, includes a discussion of the rising suicide rate. The analysis concludes that economic difficulties are not the final explanation of the rising trend. "Attention must be paid to the type of personality which we find associated with suicide rather than to place the entire emphasis upon purely external and material factors." The issue of the Bulletin for October, 1932, includes a discussion of homicide and points out that from 1911 to 1931 there has been practically no change in the death rate from this cause.

—The *Annales Medico-Psychologiques* in the issues for October and November, 1932, present an interesting discussion of the relation to tuberculosis to dementia præcox. Such discussion is based on the work of Drs. D. Hollander and Rouvroy of Belgium who presented their findings at a meeting of the Société Medico-Psychologique of Paris held November 28, 1932. These investigators conclude that there are grounds for believing that the virus of tuberculosis is found in the spinal fluid of at least certain types of dementia præcox, and that the known toxic effect of the germ is adequate to account for the damage to the central nervous system.

—Dr. David K. Henderson has been appointed physician-superintendent of the Royal Edinburgh Hospital for Mental Disorders, and professor of psychiatry in the University of Edinburgh, succeeding the late Dr. George M. Robertson. Dr. Henderson is well known in the United States, having worked with Professor Adolf Meyer at the New York State Psychiatric Institute and again at the Phipps Psychiatric Clinic of the Johns Hopkins Hospital. Prior to his present appointment, Dr. Henderson was physician-superintendent of the Gartnavel Mental Hospital in Glasgow and lecturer in psychiatry in the University of Glasgow. Dr. Henderson is joint author of a textbook of psychiatry.

—Dr. Edmund A. Christian, medical superintendent of the Pontiac State Hospital, was given a testimonial dinner in Detroit, Michigan, September 7, 1932, in honor of his 75th birthday and of his 50 years of service at the Pontiac State Hospital, of which 38 years represent his activities as medical superintendent. In commemoration of this event a bronze plaque was unveiled. This plaque, donated by Dr. Christian's more intimate friends and associates, will ultimately hang in the administration building of the Pontiac State Hospital. Dr. Christian was also the recipient of a gift volume in morocco containing about 40 letters of congratulation from his fellow life members in the American Psychiatric Association.

—In a note appearing in the *American Journal of Psychiatry*, in the issue for November, 1932, Dr. James V. May, superintendent of the Boston State Hospital, and president of the American Psychiatric Association, called attention to the rapid multiplication of societies interested in the various aspects of psychiatry. Dr. May suggests that there is an unnecessary overlapping and duplication in the activities of many of these societies and proposes that the latter consider the possibility of transforming themselves into sections of the parent organization, the American Psychiatric Association. This would make it possible for all these organizations to hold their annual meetings at the same time and place and thereby facilitate the participation of more physicians in their progress.

—The Mental Hygiene Bulletin reports in its issue for November-December, 1932, that rapid progress is being made in Argentina in the provision of facilities for mental patients. These now number about 14,000, and are cared for in seven large hospitals and ten sanatoriums. Preparations are being made for additional hospitals and psychiatric consultation centers in every province of Argentina.

Progress in mental hygiene is also reported in Spain. Since the founding of the Republic the insanity law of 1885 has been revised so as to conform to modern ideas concerning the care and treatment of mental patients; a section of psychiatry and mental hygiene has been created in the Ministry of the Interior. There is a proposal to form a council to study problems of mental hygiene.

—Robert Rosenbluth, superintendent of the New York State Training School for Boys, at Warwick, N. Y., announces the completion of the institutional medical staff, which, in cooperation with the Medical Center of Columbia University, will study methods of treating the delinquent boy. Efforts will be directed toward three main ends: the provision of adequate medical care for boys committed to Warwick; an intensive study of each individual, in collaboration with the school's department of social work; and the development of methods of dealing with criminal tendencies in children. Thorough examinations will be conducted during the quarantine period from the medical, psychiatric and social points of view. The results of these examinations will be made available to a classification committee, which will recommend the type of placement for the boy within the institution. Part of the program will consist in an academic and trade schooling. From the results of such examinations and treatment, a mass of scientific data will be assembled which it is hoped will lead to sound conclusions as to the relations of physical and mental factors to delinquency.

—A meeting of psychiatrists and psychologists of the New York State Department of Correction was held at Elmira Reformatory October 13, 1932. The discussion centered about methods of bringing the work of the Classification Clinic into more intimate relation to administrative procedure. Dr. Frank L. Christian, superintendent of Elmira Reformatory, gave the history of classification as practiced at the Reformatory during the past three decades. Dr. James L. McCartney, director of the Classification Clinic, outlined the clinical procedure. Dr. L. C. Day described the physical examinations of new inmates and Mr. I. T. Smith, the assistant superintendent, gave a layman's view of classification. The psychiatric examination was discussed by Dr. René Breguet. Dr. V. C. Branham, deputy com-

missioner of correction, concluded the program with an address on "Education and Vocation." He stated that the school of letters will be associated more closely with the trade school. A demonstration of this will be carried out at Elmira Reformatory, with the aid of a special grant, for a period of eight months. The educational program of the other correctional institutions will depend upon the results of this experiment.

—The Committee on Costs of Medical Care, organized five years ago, under the chairmanship of Dr. Ray Lyman Wilbur, secretary of the interior, has published its final report, which consists of two sets of major recommendations. The majority report, signed by 36 of the 48 members of the committee, recommends that the costs of medical care be arranged on a group payment basis, through insurance, taxation or both. Medical service, preventive and therapeutic, is to be furnished by physicians, dentists and other groups of health specialists, organized around a hospital or clinic. Each patient is to be examined by the specialists in the group, but they are to report back to an individual physician in the group who will maintain immediate personal relations with the patient. The minority report, which is supported by the American Medical Association, rejects the practice of group medicine and urges the restoration of the general practitioner to the principal post in medical practice.

A new organization, the American Committee on Medical Costs, has been formed to support the majority report. This committee includes Morris L. Cooke, director of the Germantown Hospital, Philadelphia, chairman; Dr. Livingston Farrand, president of Cornell University; Dr. Michael Davis, of the Julius Rosenwald Foundation; Evans Clark, of the Twentieth Century Fund and William J. Schieffelin, president of the Druggists Supply Corporation.

—The twenty-third annual meeting of the National Committee for Mental Hygiene was held on November 10, 1932. Dr. C. M. Hincks, the general director, spoke on the relation of the economic depression to the mental health of the people and pointed out that current rates of admission to mental hospitals do not provide a significant index of the prevalence of mental disease. The effects of the depression on mental health may not become apparent for many years. The following speakers also addressed the meeting: Dr. George S. Stevenson, director of the division on community clinics; Willoughby G. Walling, chairman of the Illinois Board of Public Welfare Commissioners; Dr. Arthur H. Ruggles, superintendent of Butler Hospital, Providence, R. I., and Clifford W. Beers. The meeting was followed by the election of officers for the ensuing year. The following offi-

cers were re-elected: Honorary president, Dr. William H. Welch of Baltimore; president, Dr. Charles P. Emerson of Indianapolis; vice presidents, President James R. Angell of Yale University, Dr. William L. Russell of New York, Dr. Bernard Sachs of New York; general director, Dr. C. M. Hincks; treasurer, Frederic W. Allen; and secretary, Clifford W. Beers. Dr. Arthur H. Ruggles of Providence was re-elected chairman of the Scientific Administration Committee; Dr. Augustus Knight of New York, chairman of the executive committee; and Mortimer N. Buckner of New York, chairman of the finance committee.

—Dr. M. Allen Starr, distinguished neurologist, died in Marienbad, Germany, September 4, 1932, at the age of 78. He was born in Brooklyn, N. Y., and received his early schooling in Orange, N. J. He graduated from Princeton University at a time when his interests had been greatly stimulated by a knowledge of the great advances being made in the field of brain localization. He pursued these studies in Germany under Helmholtz and Wundt and turned his mind definitely towards medicine. He entered the College of Physicians and Surgeons of Columbia University and graduated in 1880. More post-graduate study in neurology followed in Europe where he studied, among others, with Meynert and Chareot. An essay on the sensory tract in the nervous system published in 1884 won him the Alumni Association Prize of the College of Physicians and Surgeons, and led to his appointment as professor of anatomy and physiology of the nervous system at the New York Polyclinic. In 1886 he became professor of nervous diseases, but resigned in 1889 to become professor of nervous diseases at the College of Physicians and Surgeons, holding the latter post until 1917, when he became professor emeritus. Dr. Starr received the degrees of B. A., M. A., Ph. D., and LL.D., from Princeton University and the degree of Sc. D., from Columbia University. He was president of the American Neurological Association in 1896, of the New York Neurological Society in 1894-97 and vice president of the New York Academy of Medicine, 1903-06. He was a foreign member of the neurological societies of London, Paris, Berlin and Vienna. He was the author of a number of books and of many articles dealing with nervous and mental diseases.